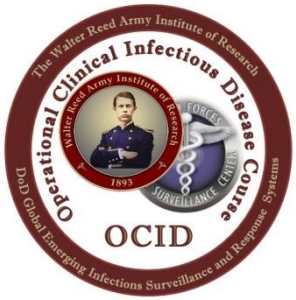
Rickettsial Diseases and friends….

WRAIR- GEIS 'Operational Clinical Infectious Disease' Course



Acknowledgments

- MAJ Jason M. Blaylock, MD
- LTC Josh Hartzell,MD

July 2015

Disclaimer

The views expressed in this presentation are those of the speaker and authors, and do not reflect the official policy of the Department of Army, Department of Defense, or U.S. Government

Objectives

- Familiarization with:
  - Classification
  - Geographic distribution
  - Vector transmission
  - Clinical presentations
  - Disease specific features (risk factors, treatment)
- Clinical case exercises

Common Rickettsial Infections

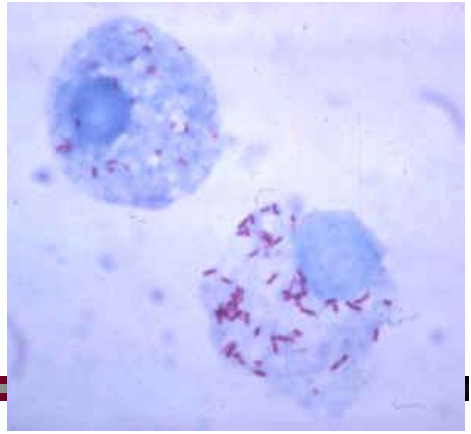
Rickettsiae

	Tick-Borne	Flea-Borne	Louse-Borne	Mite-Borne
Spotted Fever Group	*R. rickettsii*			
	R. conorii			
	R. japonica	*R. felis*		*R. akari*
	R. africae			
	R. parkeri			
Typhus Fever Group		*R. typhi*	*R. prowazekii*	
Scrub Typhus				*O. tsutsugamushi*
Anaplasma	*A. phagocytophilum*			
Ehrlichia	*E. chafeensis*			
	E. ewingii			
	E. canis			
Q Fever	*Coxiella burnetii*			
Lyme disease	*Borrelia burgdorferi*			

What's in Common?

- Obligate intracellular Gm-negative bacteria
- Transmission
  - Ticks, fleas, lice, mites (chiggers)
- Incubation: 1-2 weeks
- Non-specific symptoms
- Broad spectrum: mild flu-like to very ill
- ↓platelets, ↓ WBCs, ↑ liver tests

- **Doxycycline is effective!**



Common things being common

Destination	No. travelers						
	SFG rickettsiosis	TG rickettsiosis	Indeterminate SFG/TG rickettsiosis	Scrub typhus	Anaplasmosis	Acute Q fever	Bartonellosis
Western Europe	7	1			1	2	1
Eastern Europe			1				
North Africa	3						
Sub-Saharan Africa	197	1				5	1
Middle East	1					2	1
Northeast Asia	2	1				1	
South central Asia	5	1	1	5			
Southeast Asia	3	6	2	9			1
Australia/New Zealand	1			1			
Oceania	1						
North America	1						
Central America	3						
Caribbean	1						3
South America							
Unknown	6			1		1	
Total	231	10	4	16	1	11	7

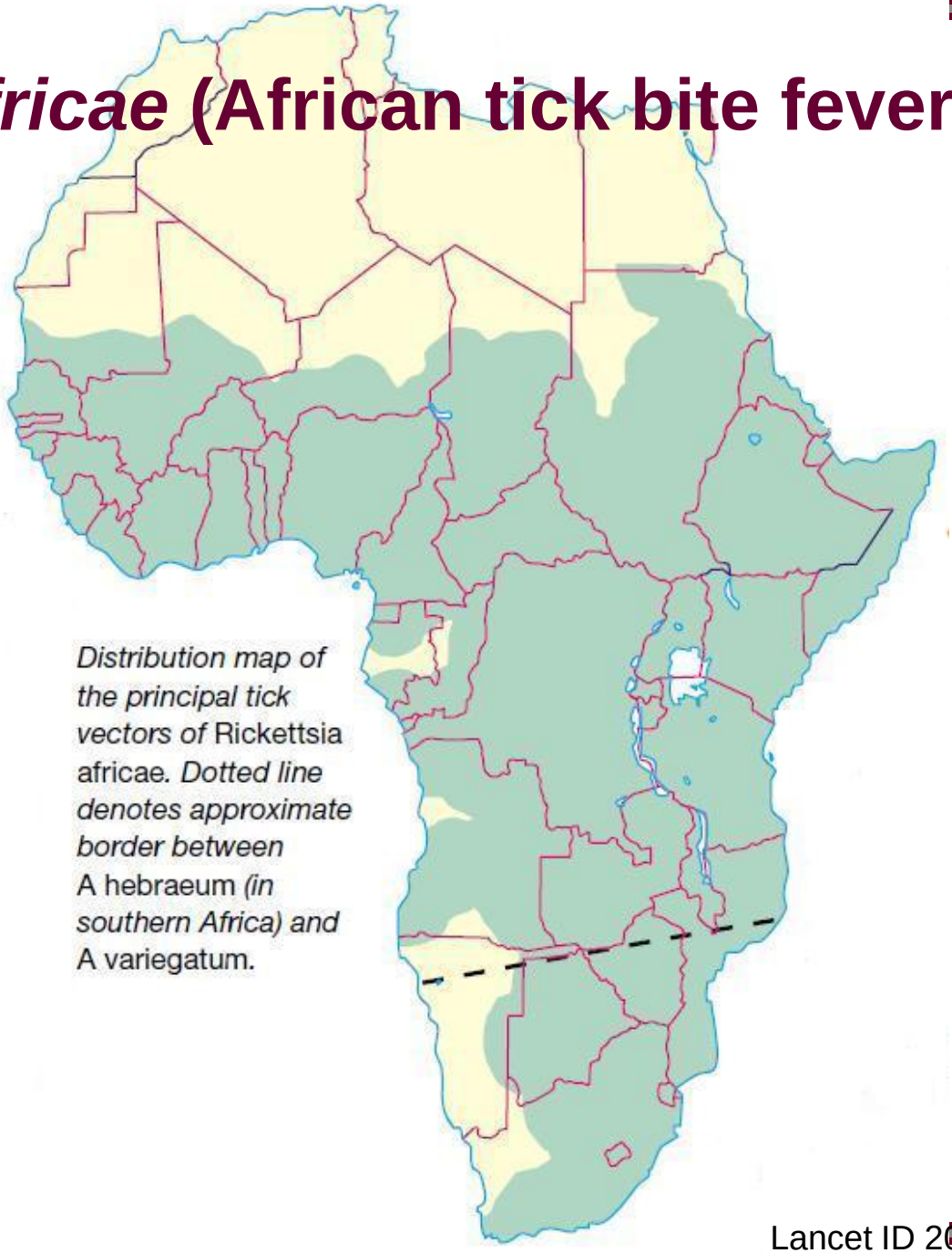
*SFG, spotted fever group; TG, typhus group.

EID 2009;15(11):1791-1798.

Spotted fever group

Tick	Flea	Mite
R. rickettsii	*R. felis*	*R. akari*
R. conorii		
R. japonica		
R. africae		
R. parkeri		

R. africae (African tick bite fever)



Distribution map of the principal tick vectors of Rickettsia africae. *Dotted line denotes approximate border between* A hebraeum *(in southern Africa) and* A variegatum.

Lancet ID 2003:557-564

R. africae (African tick bite fever)

- Incubation 5-7 days
- Acute, febrile, and influenza-like illness
  - Severe headache, nausea, fatigue
  - Prominent myalgias (esp. neck)
- Inoculation eschar(s)
  - Black crusts surrounded by a red halo
- +/- vesicular rash/aphthous ulcers
- Regional lymphadenitis
- ~50% of patients have multiple eschars
- Rare complications; recovery is the rule

Lancet ID 2003;3:557-564

R. africae (African tick bite fever)

Lancet ID 2003;3:557-

R. africae (African tick bite fever)

- Habitat: tall grasses/bush; shade; rainy season
- Risks: soldiers, safaris, campers, farmers
  - Aggressive: single host attacked by several ticks, multiple times
- Diagnosis: difficult (clinical)
- Treatment: Doxycycline 100mg BID 7d or until 48hrs post defervescence
- Prevention: PPE; skin exam, careful tick removal

R. conorii (Mediterranean spotted fever *AKA* Boutonneuse fever)

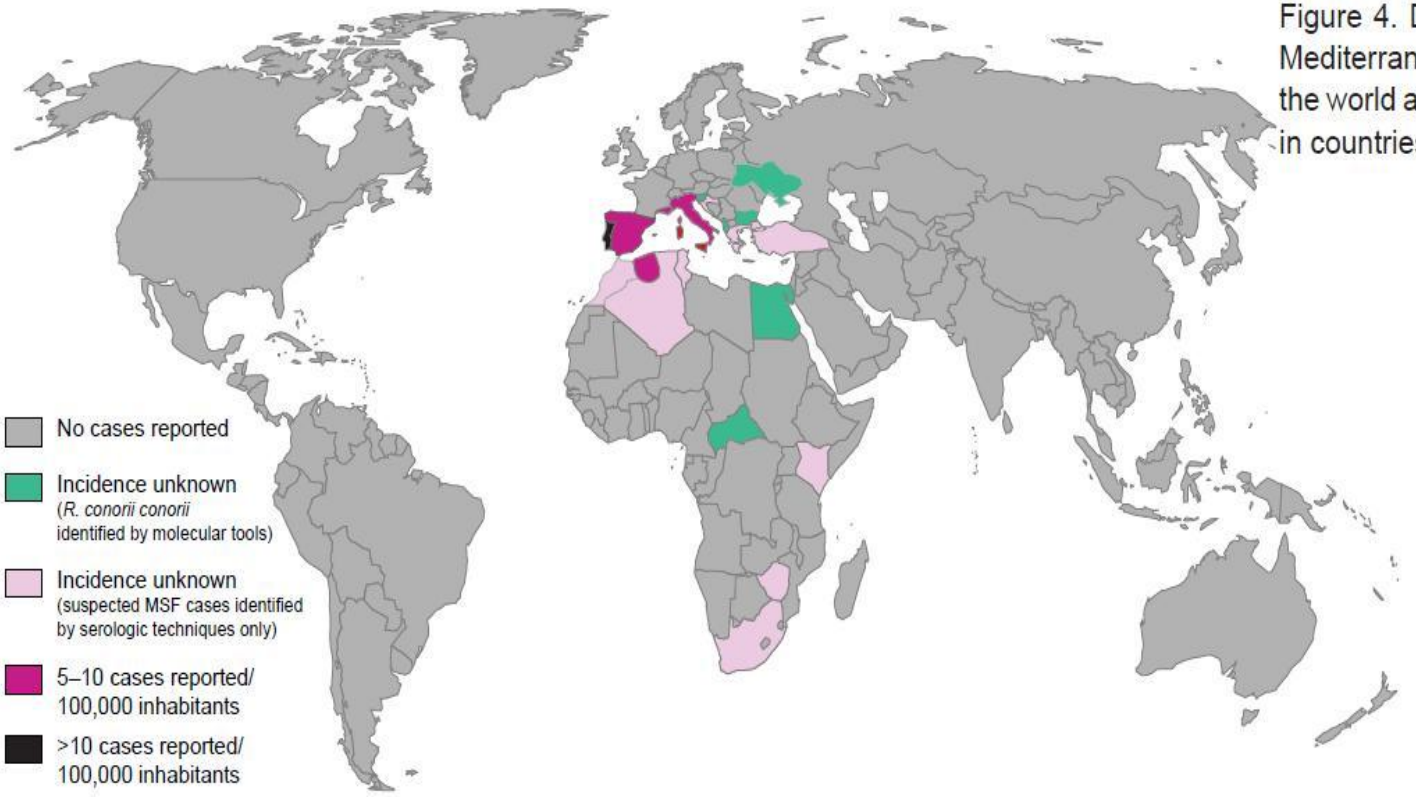


Figure 4. Distribution of the cases of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.

EID. 2008;14(9):1360-1367

R. conorii (Mediterranean spotted fever *AKA* Boutonneuse fever)

Rickettsia	Vector t	Symptoms present, % patients: Fever	Inoculation eschar	Rash	Fatal forms? (% patients)	nt, % patients: on Rash	Fatal forms? (% patients)
R. conorii conorii, isolates Malish, Moroccan Kenyan	*Rhipicepl* sp., *Haemaph* *leach*	91–100	20–87	93–100	Yes (0–18.1)	93–100	Yes (0–18.1)
R. conorii israelensis	*Rh. sang*					98–100	Yes (0–3.5)
R. conorii caspia	*Rh* *sanguine* *pumi*					94	No
R. conorii indica	*Rh* *sanguir* *Booph* *microplu* *leac*					100 (frequently purpuric)	No
		100	Rare	100 (frequently purpuric)	No		

Unlike African tick bite fever, eschars RARELY multiple in MSF

EID. 2008;14(9):1360-136

R. conorii (Mediterranean spotted fever *AKA* Boutonneuse fever)

- Incubation 5-7 days
- Fever, HA, maculopapular rash; tache noire
- Ecology of exposure: peridomestic; buildings where dogs kept
- Diagnosis tough
  - Clinical +/- biopsy (eschar); serology (IFA), PCR, culture
- Treatment: Doxy 100mg BID 5-10 days
- Prevention: PPE

EID. 2008;14(9):1360-136

Rocky Mountain Spotted Fever

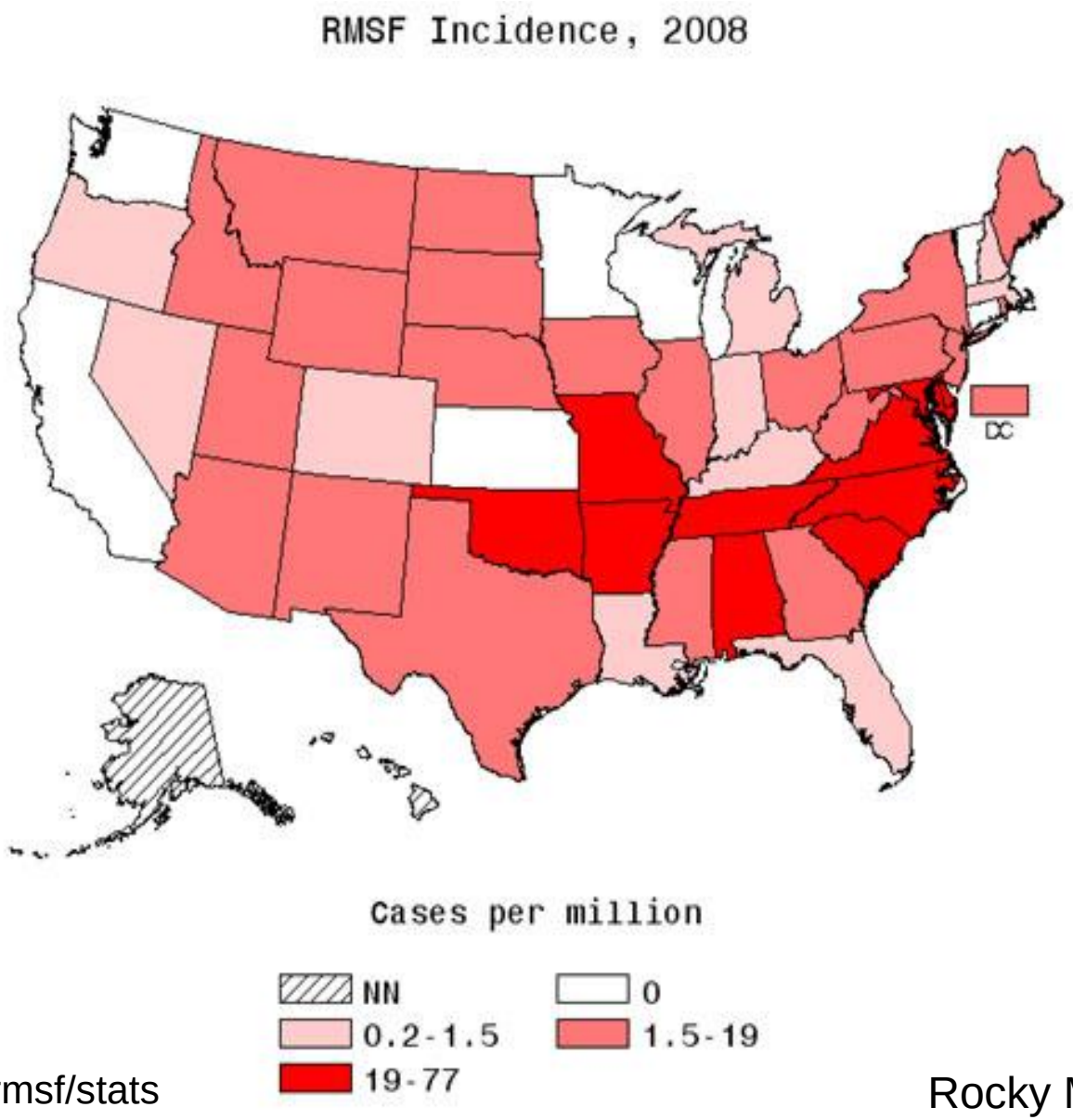
- RMSF, *R. rickettsii*
- USA, southern Canada, C/S Americas
- Vector
  - *Dermacentor variabilis* (American dog tick)
  - *D. andersoni* (Rocky Mountain wood tick)

- Minimum attachment: 4-6hrs
- Incubation: 2-14 days

RMSF Rash

cdc.gov/rmsf/symptoms

RMSF



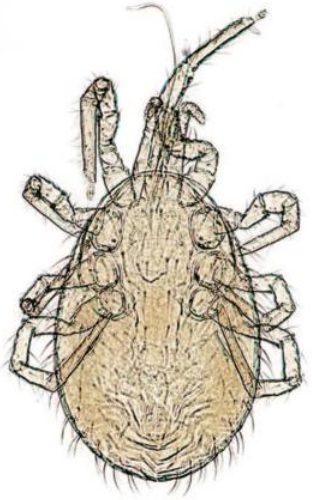
American dog tick

Rocky Mountain Wood tick

cdc.gov/rmsf/stats

R. akari (Rickettsialpox)

- Morphologically identical to *R. rickettsii*
- Vector: house mouse mite
- Reservoir: common house mouse
- “urban zoonosis” since 1950s
  - NYC, Boston, West Hartford, Philadelphia, Pittsburgh, Cleveland
- Worldwide: Russia, Korea, South Africa



J Am Acad Dermatol Nov 200

R. akari (Rickettsialpox)

- Incubation 7-10 days
- Painless bite
- Papulovesicle -> eschar within 1-2 days
- Fever, malaise 1 week later
- Diffuse papulovesicular rash 2-3 days after fevers
  - Trunk, extremities, oral mucosa
- Generalized lymphadenopathy
- Self-limited (7-10 days after symptom onset)

Rickettsialpox

J Am Acad Dermatol
2004;51:S137-42
healthfiles.net/disease/category/r

R. akari (Rickettsialpox)

- Labs: mild leukopenia; thrombocytopenia, mild proteinuria
- Definitive Dx: rise in serum *R. akari* Ab during convalescence (CF, IFA)
  - Cross-reactive with RMSF Ab
- Treatment: Doxycycline 100mg BID until clinically improved for 48hrs (~ 5-7 days)
- Prevention: PPE

"Pox" DDX

Feature	Rickettsialpox	Chickenpox[24]	Smallpox (variola major)[25]
Eschar	Yes	No	No
Incubation period	9-14 days	14 days (range 10-23)	12 days (range 10-14)
Prodrome	Usually mild, may be severe. Fever, malaise, and headache.	Absent or mild and brief (less than one day)	Usually severe with high fever, headache, backache. Vomiting and severe abdominal pain may be present. Lasts 2 to 4 days.
Timing and evolution of lesions	Lesion develops at the site of the bite within 24 to 48 hrs and evolves into eschar. Rash begins 2 to 3 days after prodrome. Papules may eventuate in papulovesicles.	Lesions occur in "crops" over 2 to 4 days. Different stages characteristic: macules, papules, vesicles, pustules, crusts	Emerge over 1-2 days and then progress at same rate. The lesions progress over several days from macules (day 1), to papules (day 2), to vesicles (days 3-5), to pustules (days 7-14), to scabs (day 14-20).
Pruritus/ pain	Exanthem usually asymptomatic: occasional pruritus.	Commonly pruritic	Pruritic during healing, otherwise may be painful.
Distribution	Anywhere. Palms, soles not usually involved.	Starts on trunk and face and spreads centrifugally. Palms, soles may be involved	Begins on the oral mucosa, face, and extremities and spreads centripetally. Palms, soles commonly involved.
Enanthem	Minority of cases.	Common, especially palate.	Starts in mouth
Scarring	Eschar leaves depressed scar, papulovesicles do not.	If bacterial superinfection occurs	Yes

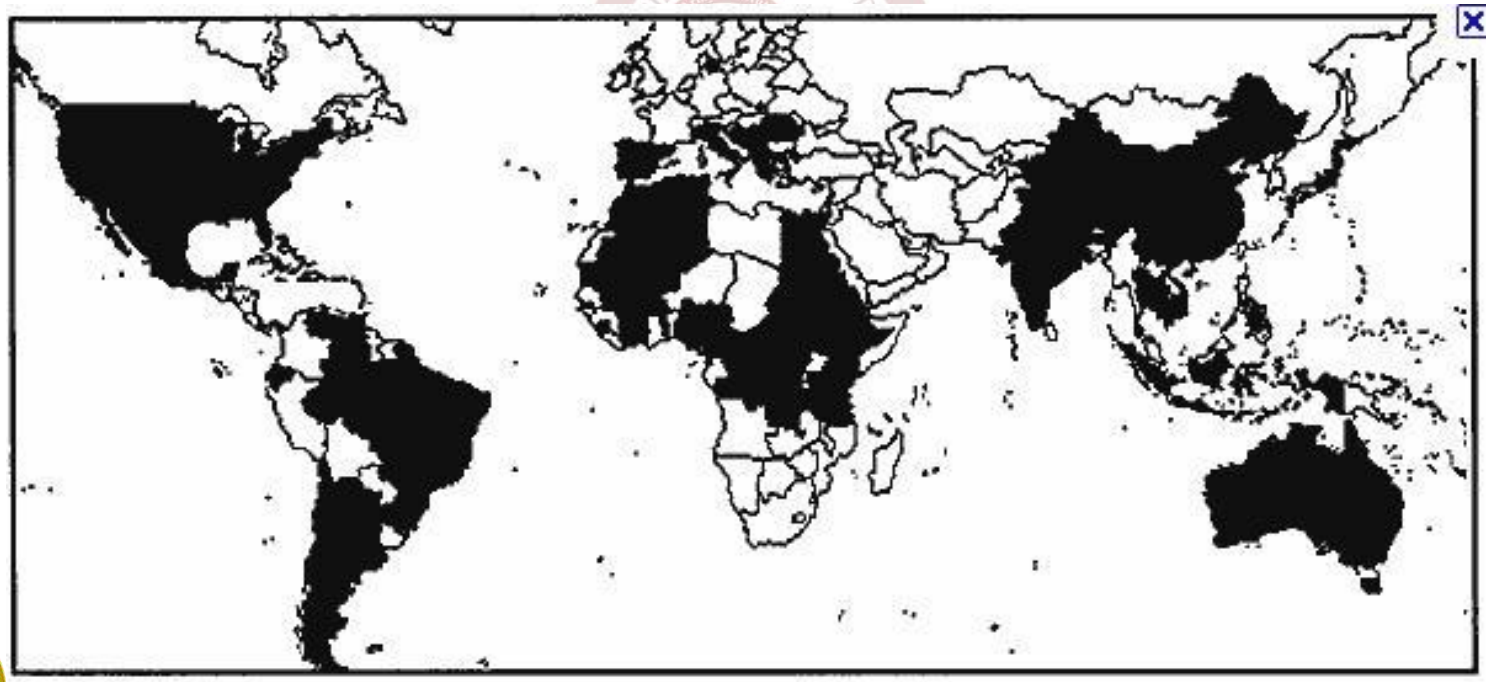
J Am Acad Derm. 2004;51(5)S137-S142

Typhus group

Flea	Louse	Chigger mite
R. typhi	***R. prowazekii***	
		O. tsutsugamushi

R. typhi (murine/endemic typhus)

- Found sporadically worldwide
  - In US: Hawaii, California, Texas
- Hosts: Rats, cats, mice Vector: fleas



WHO, 1998

EID. 1998;4(4):677-680

R. typhi (murine/endemic typhus)

- Flea bites (infected feces contaminate skin) or aerosolization
- Incubation 6-14 days
- Fever, headache, rash (triad in 50%)
- Leukocytosis or mild leukopenia
- Anemia (severe with G6PD def)
- +/- ↓Na, hepatic/renal abnormalities

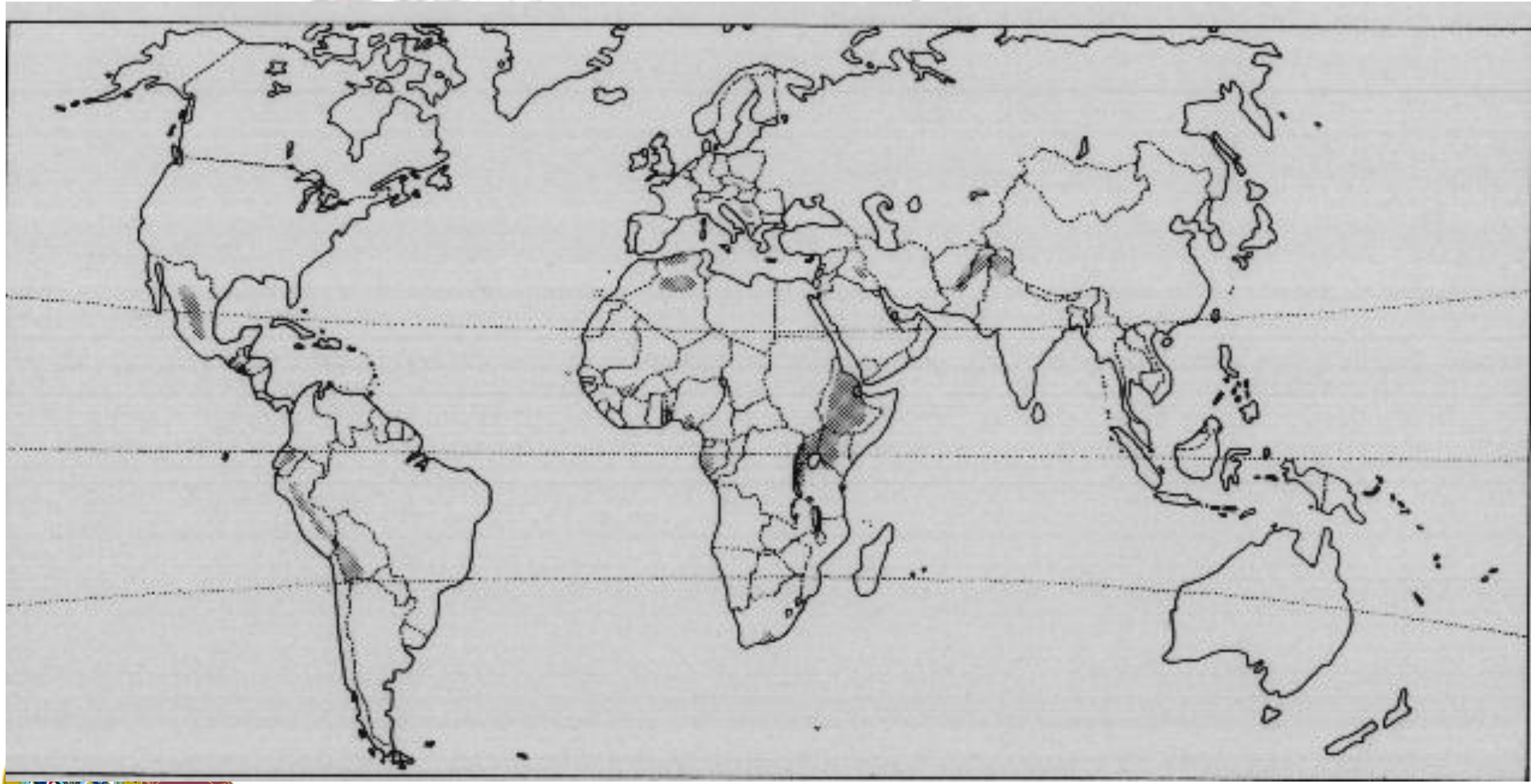
CID 2013; 46(6):913-918.

R. typhi (murine/endemic typhus)

- Ecology: Rat fleas; coastal areas
- Diagnosis (clinical): serology (IFA)
  - Cross-reative with *R. prowazekii* and RMSF Ab
- Spontaneous recovery in 2 weeks
- Treatment: Doxycycline 100mg BID for 48-72hrs after fever resolved
- Prevention: PPE

CID 2013; 46(6):913-918.

R. prowazekii (louse-borne/epidemic)



WHO, 1998

R. prowazekii (louse-borne/epidemic)

- Incubation 6-14 days
- Fever, headache (abrupt), tachypnea, myalgias
- Rash (mac-pap/petechial) on days 4-7
  - Spreads peripherally (unlike RMSF)
- CNS disease: confusion, drowsiness, coma
- Shock: multifocal/multi-organ vasculitis
  - Mortality 60% w/o abx; 4% w/ abx
- Recrudescence (Brill-Zinsser disease)
  - Mild illness, elderly, years after initial episode

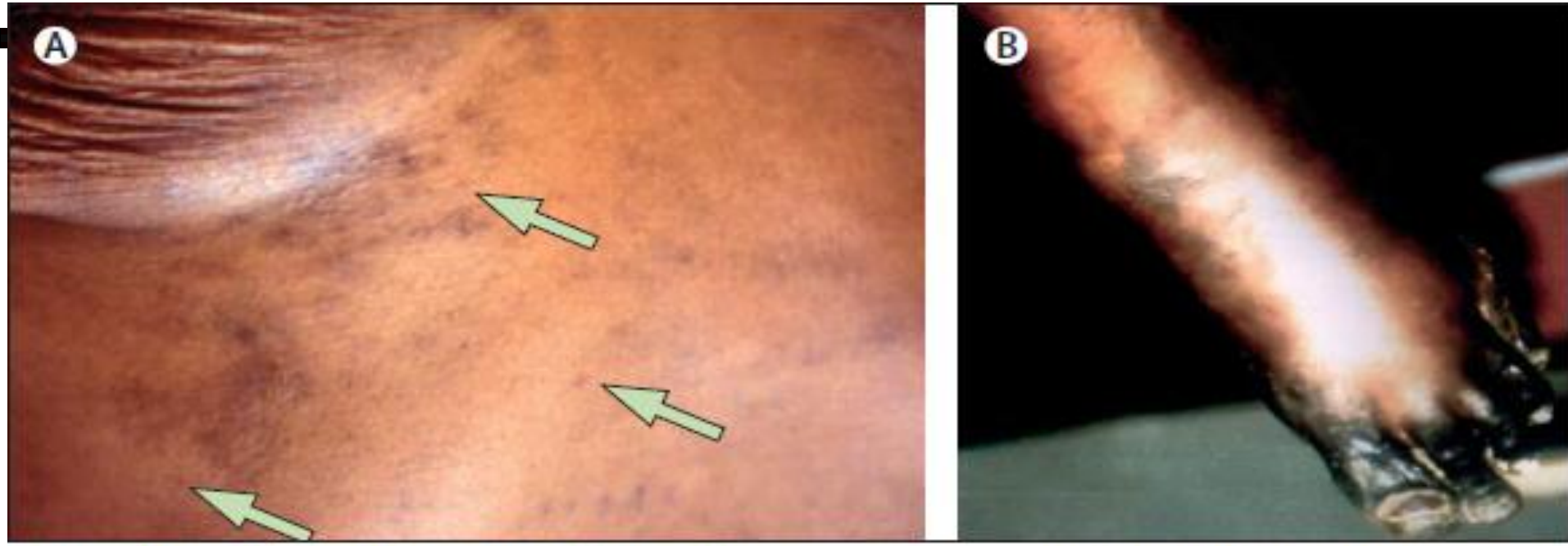


Figure 4: (A) Skin rash and (B) toe gangrene in a patient infected with epidemic typhus during Burundi outbreak, 1997

Figure 1: Scratching lesion on the upper arm of a homeless man

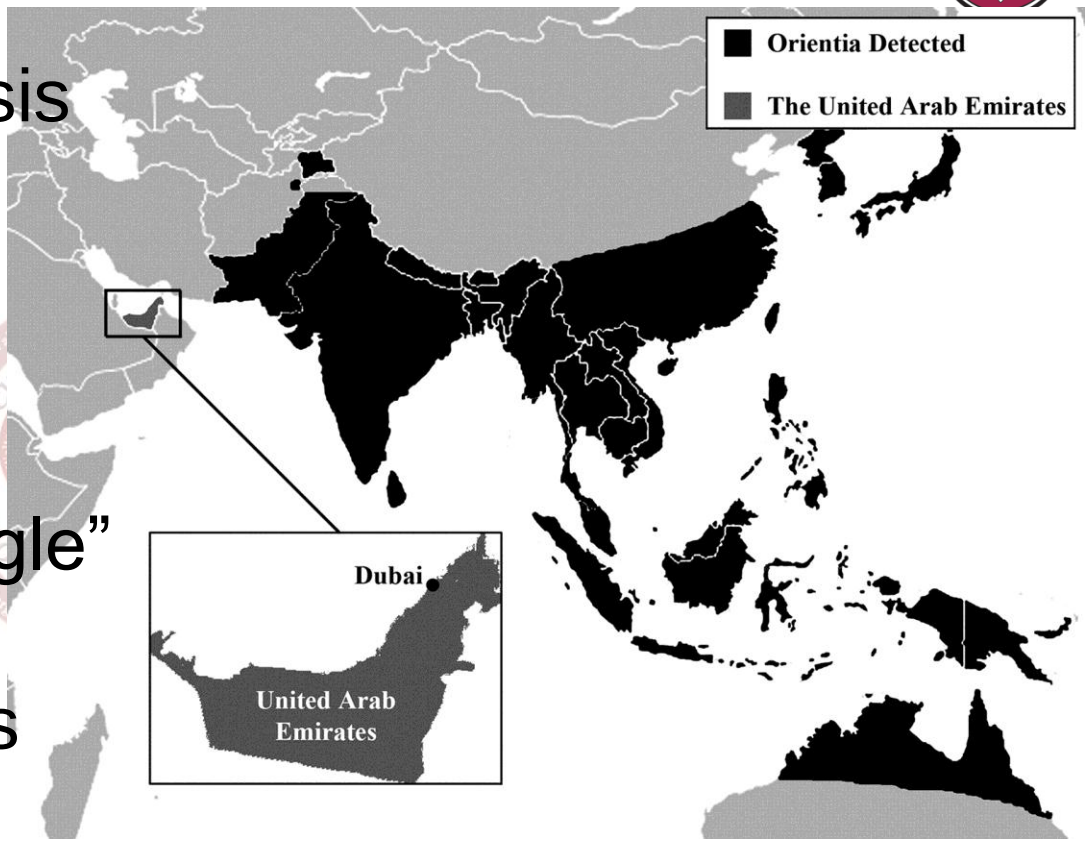
se 2015

R. prowazekii (louse-borne/epidemic)

- Vector: body louse *(Pediculosis humanus)*
- Reservoir: humans
  - Flying squirrels
- Ecology: crowded, war/disasters, famine, poverty
- Diagnosis: serology (IFA), biopsy, PCR
- Treatment: Doxycycline (as endemic)
- Prevention: delousing (permethrin>lindane, malathion)
  - Boiling clothes, bedding
  - Long-acting insecticides
  - Prophylaxis (doxycycline)

O. tsutsugamushi (Scrub typhus)

- Chigger-borne zoonosis
- Vector: larval mites
  - "mite islands"
- "Tsutsugamushi Triangle"
  - Tropical Asia
  - west Pacific islands
  - UAE

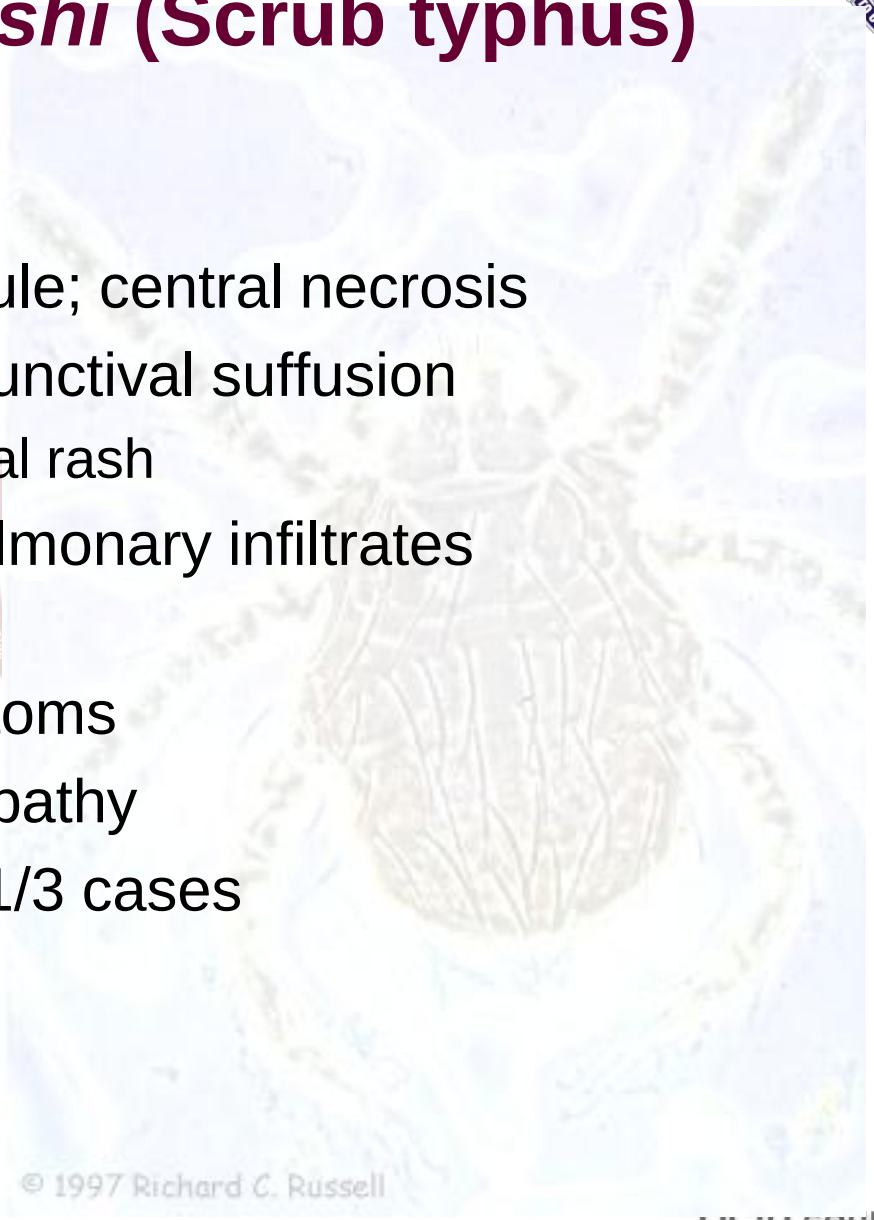


Izzard L et al. J. Clin. Microbiol. 2010;48:4404-4409

EID. 1997;3(2):105-111

O. tsutsugamushi (Scrub typhus)

- Painless bite
- Eschar - painless papule; central necrosis
- Fever, chills, HA, conjunctival suffusion
  - All prior to centrifugal rash
- Cough, tachypnea, pulmonary infiltrates
  - Most common
- Gastrointestinal symptoms
- Regional lymphadenopathy
- Acute hearing loss in 1/3 cases
- CFR 10% if untreated

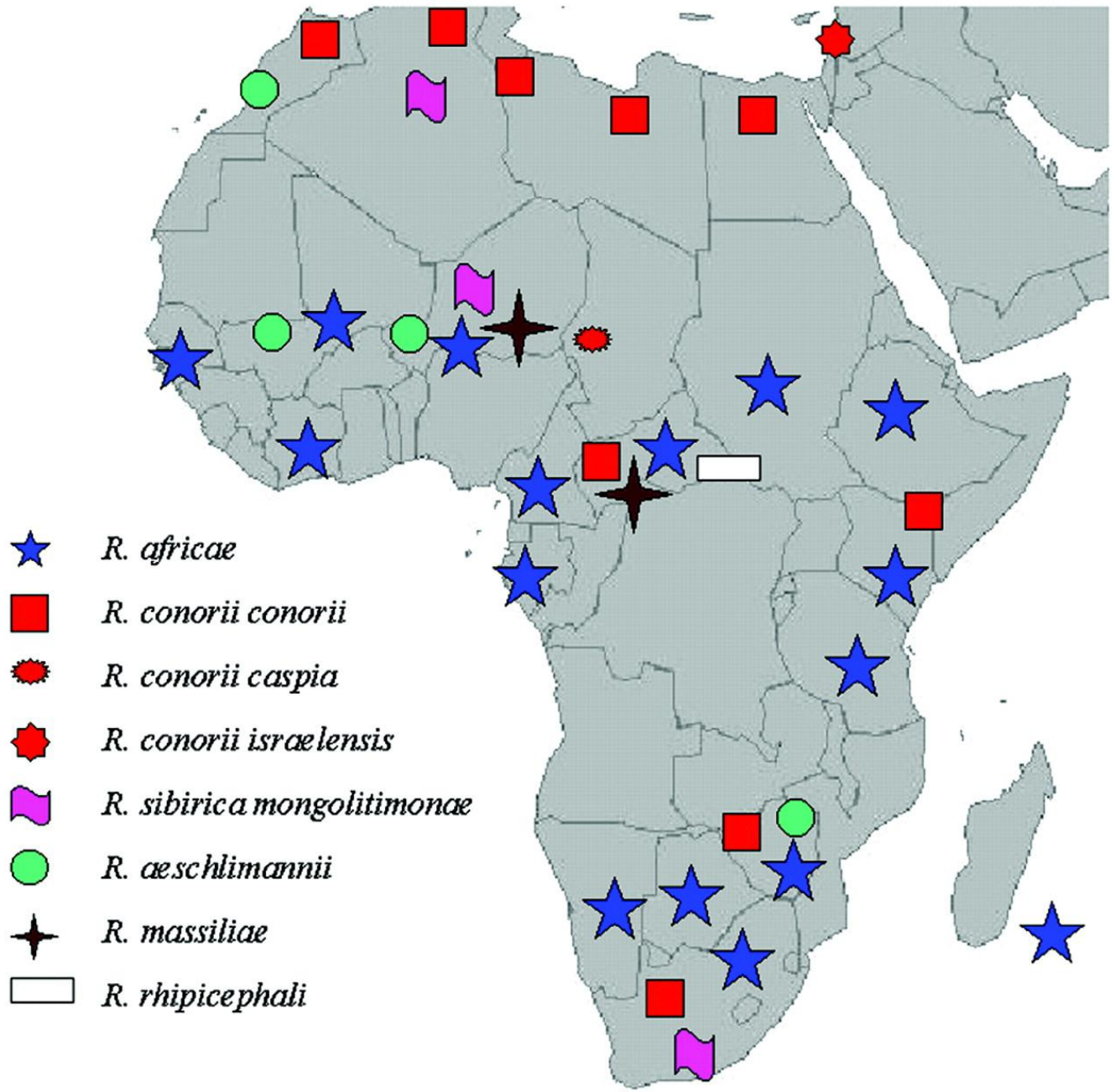



history.amedd.army.mil

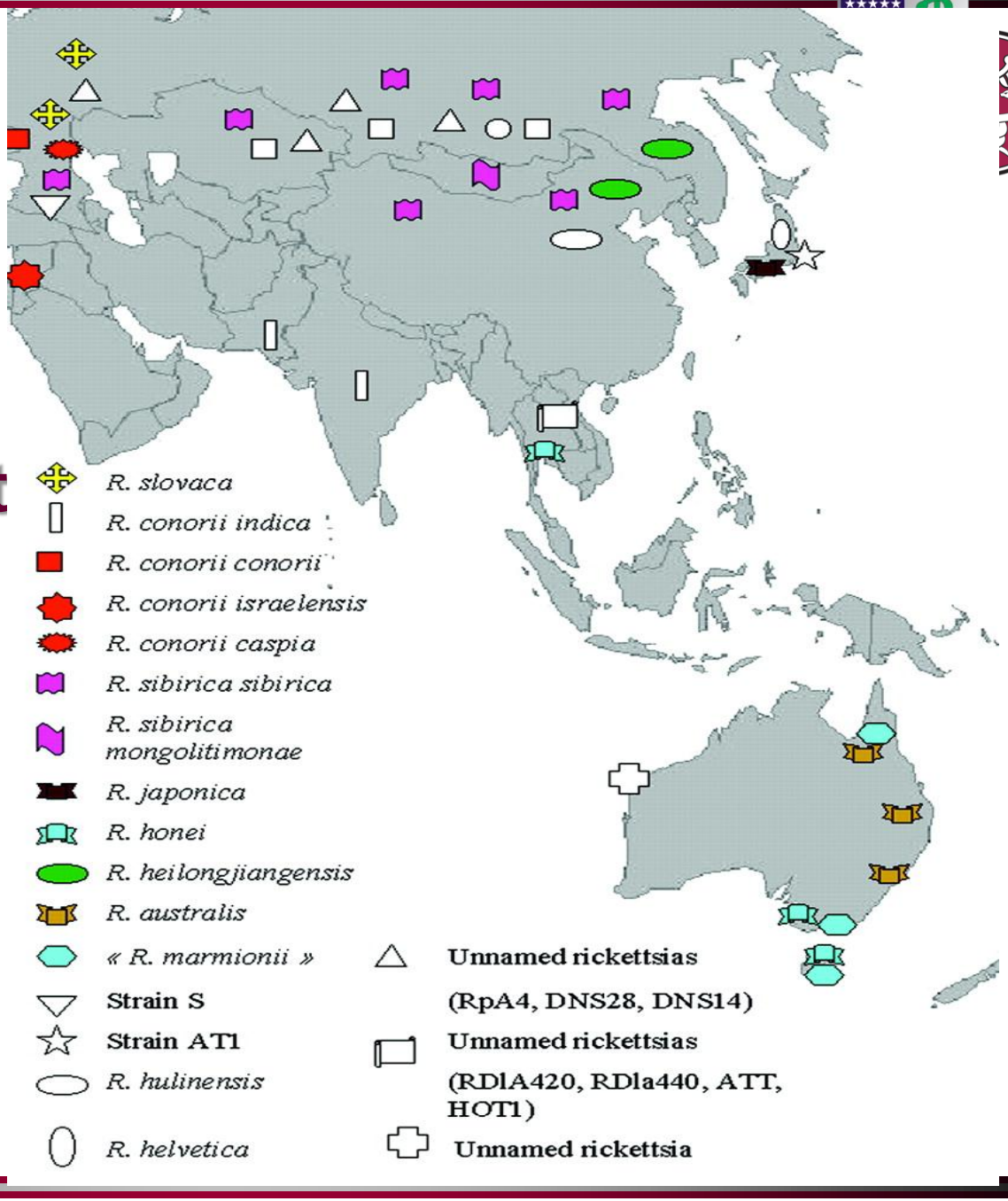
O. tsutsugamushi (Scrub typhus)

- Ecology: active rice fields, agricultural areas, warm humid tropics
- Rats key to population densities
- Diagnosis: clinical; IFA gold standard; PCR, isolation in blood
- Eschar in SE Asia pathognomonic
- Treatment: Doxycycline (resistance possible)
  - Azithromycin, rifampin
- Prevention: topical repellents to clothing, weekly doxycycline

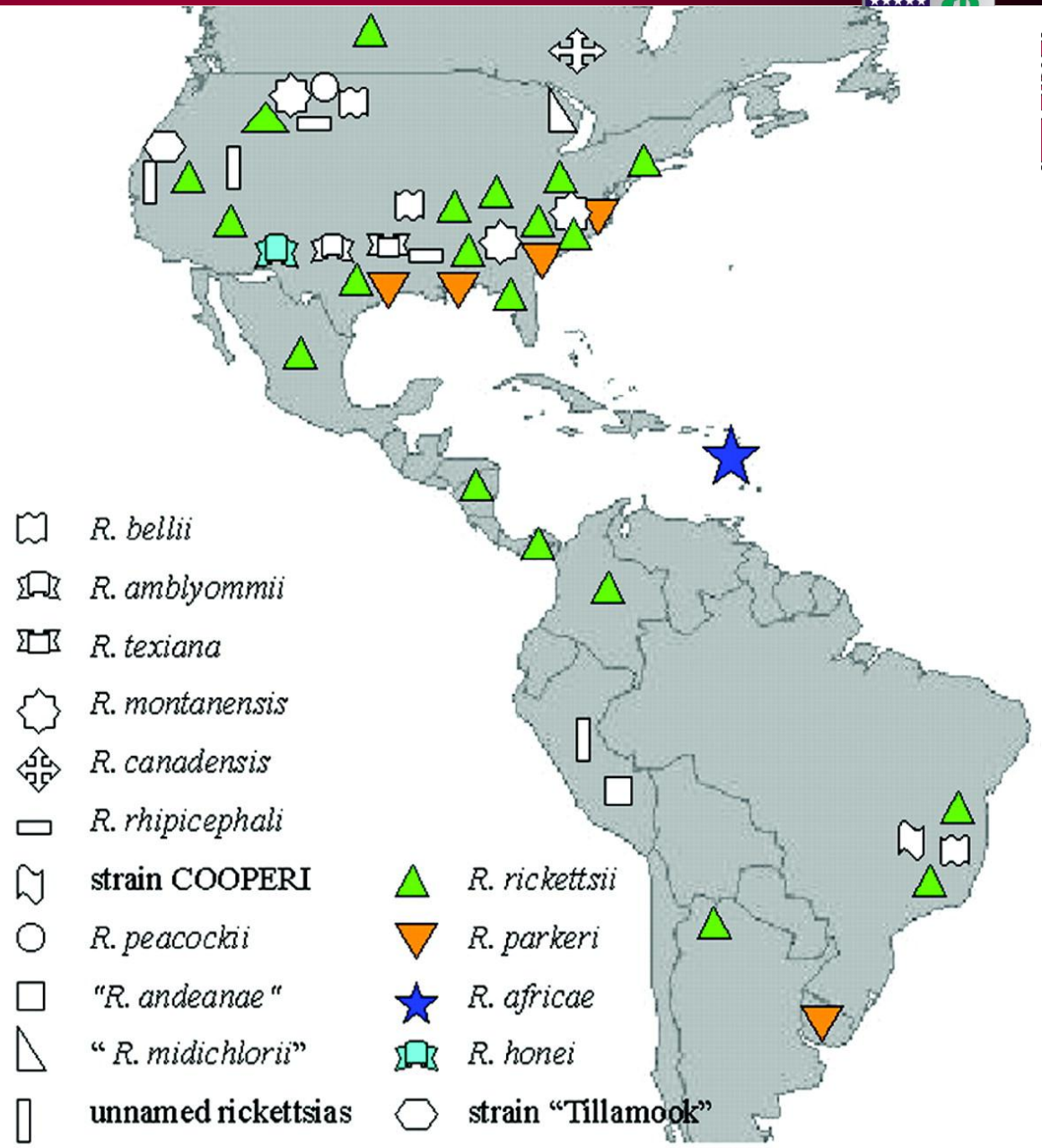
Tick-Borne Rickettsiae in Africa



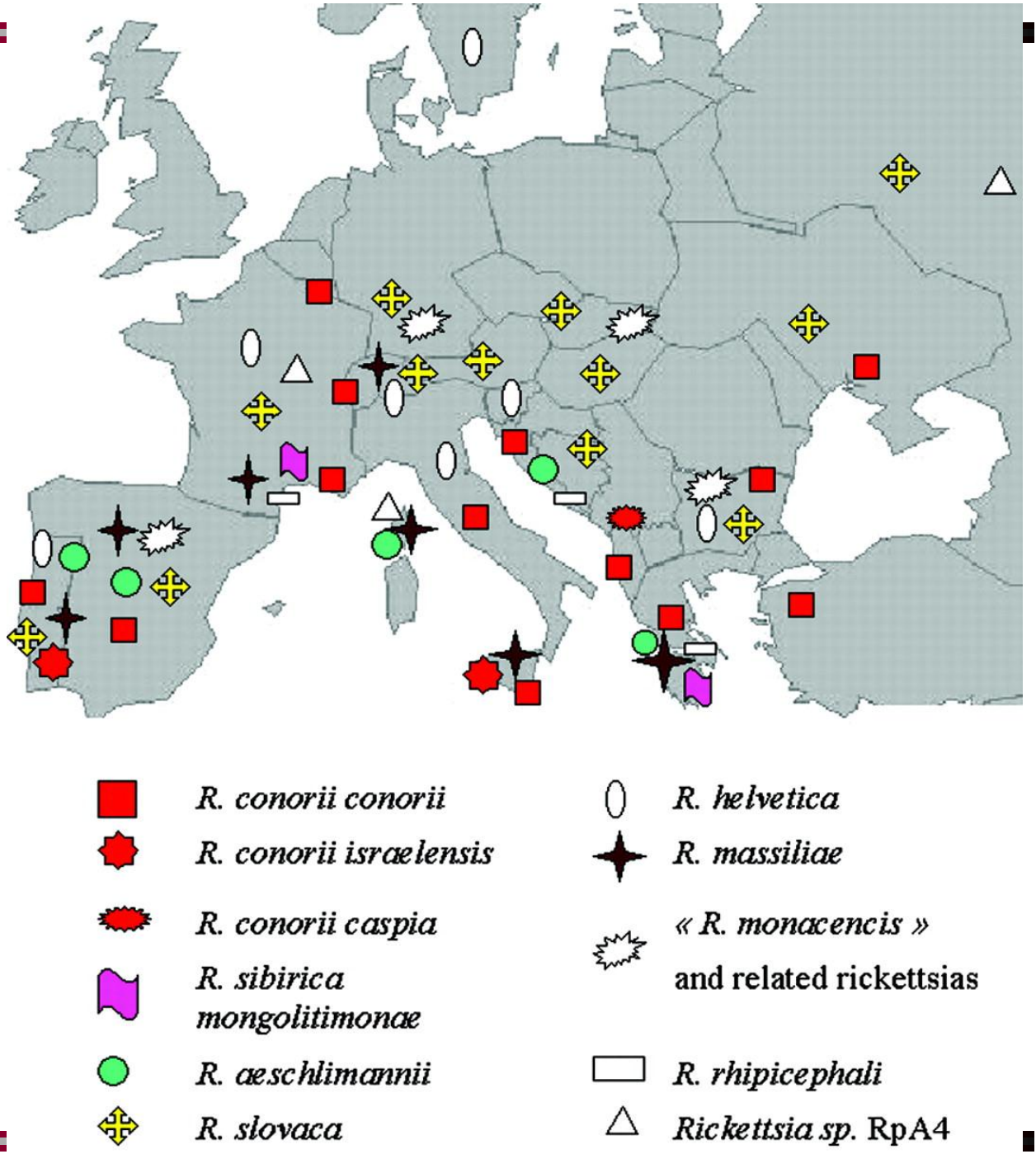
Tick-Borne Rickett in Asia/Australia



Tick-Borne Rickettsiae in the Americas



Tick-Borne Rickettsiae in Europe



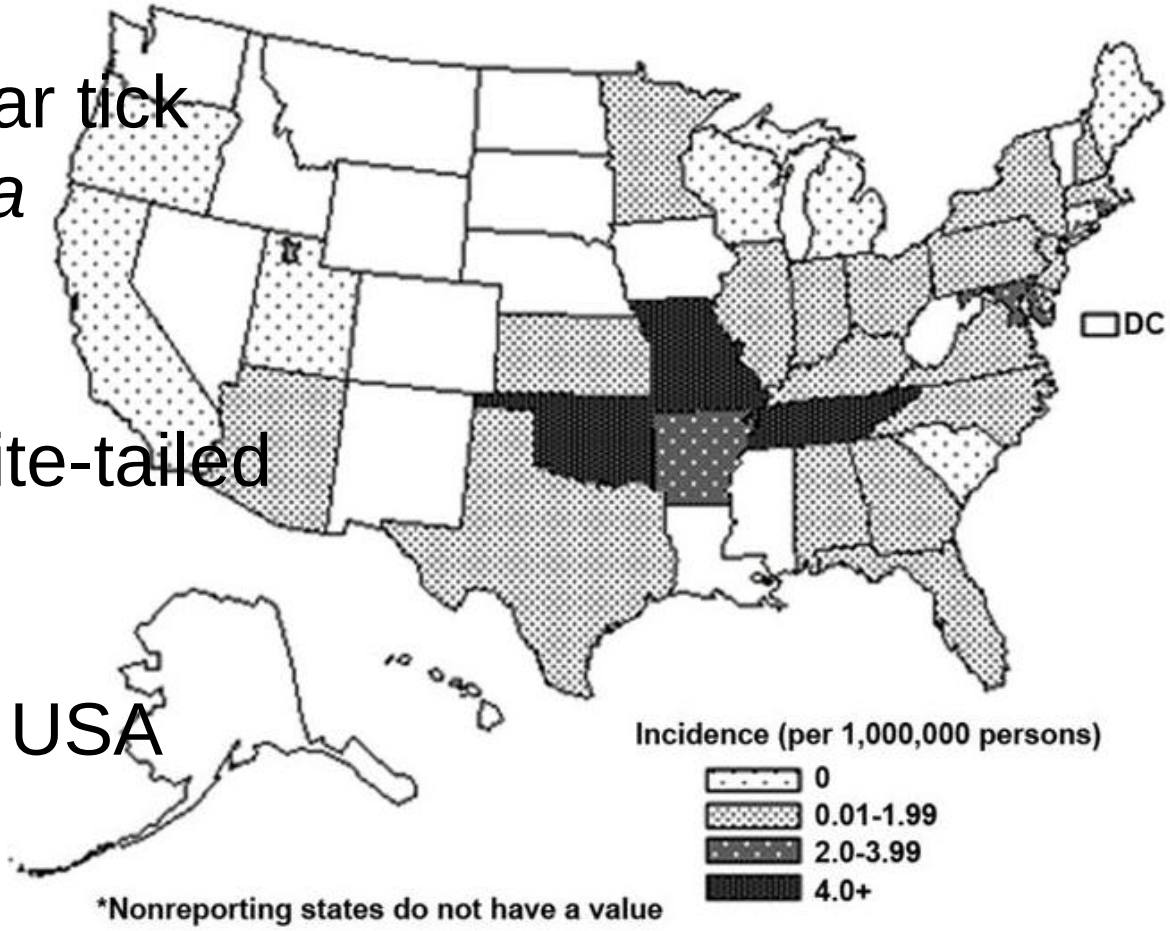
"Ehrlichiosis"

HME	HGA	*E. ewingii*
1987	1994	1999
E. chaffeensis	*A. phagocytophilum*	*E. ewingii*
Monocyte macrophage	Granulocyte	Granulocyte
>1600 cases/yr	>2100 cases/yr	~20 (immunocompromised)
SC, SE, mid-Atl	NE, MW, Pac coast	SC

Dumler JS, Walker DH. *Ehrlichiosis and Anaplasmosis* inTropical Infectious Diseases 2006.

HME Distribution

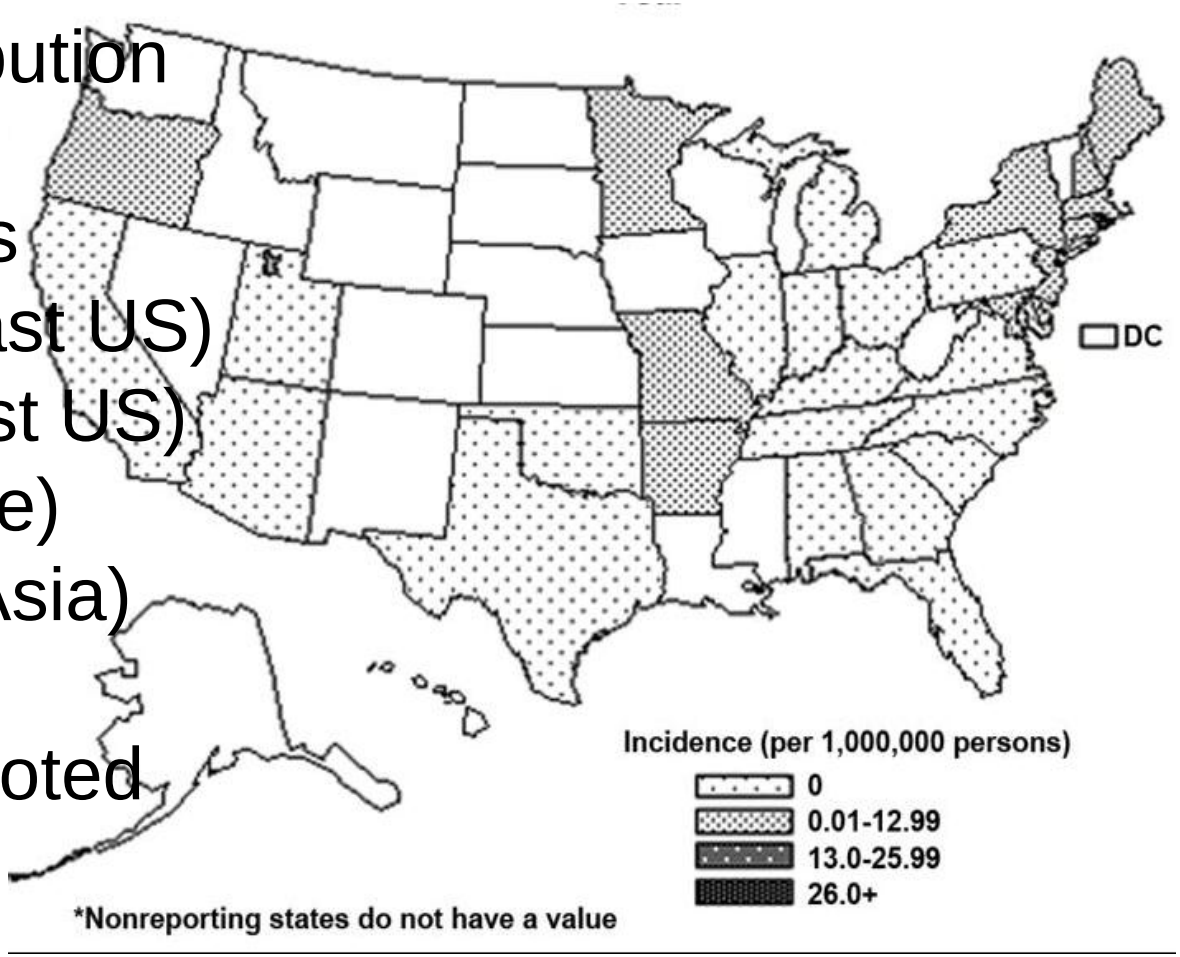
- Vector: lone star tick
  - *Amblyomma americanum*
- Reservoir: White-tailed deer
- Only occurs in USA



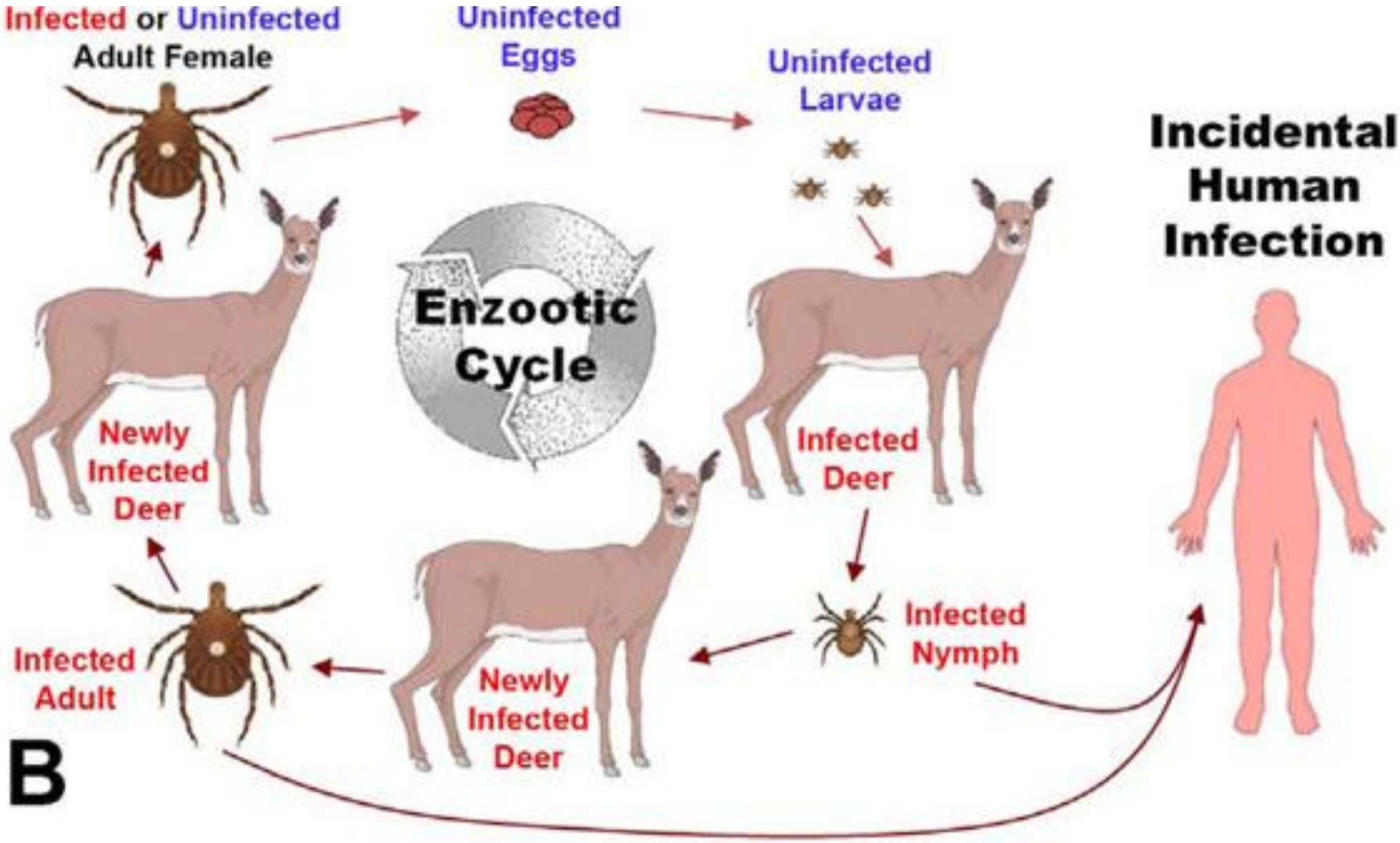
Clin Lab Med March 2010

HGA Distribution

- International distribution
- Vector: *Ixodes* ticks
  - *I. scapularis* (East US)
  - *I. pacificus* (West US)
  - *I. ricinus* (Europe)
  - *I. persulcatus* (Asia)
- Reservoir: white-footed mouse



Anaplasma Life Cycle



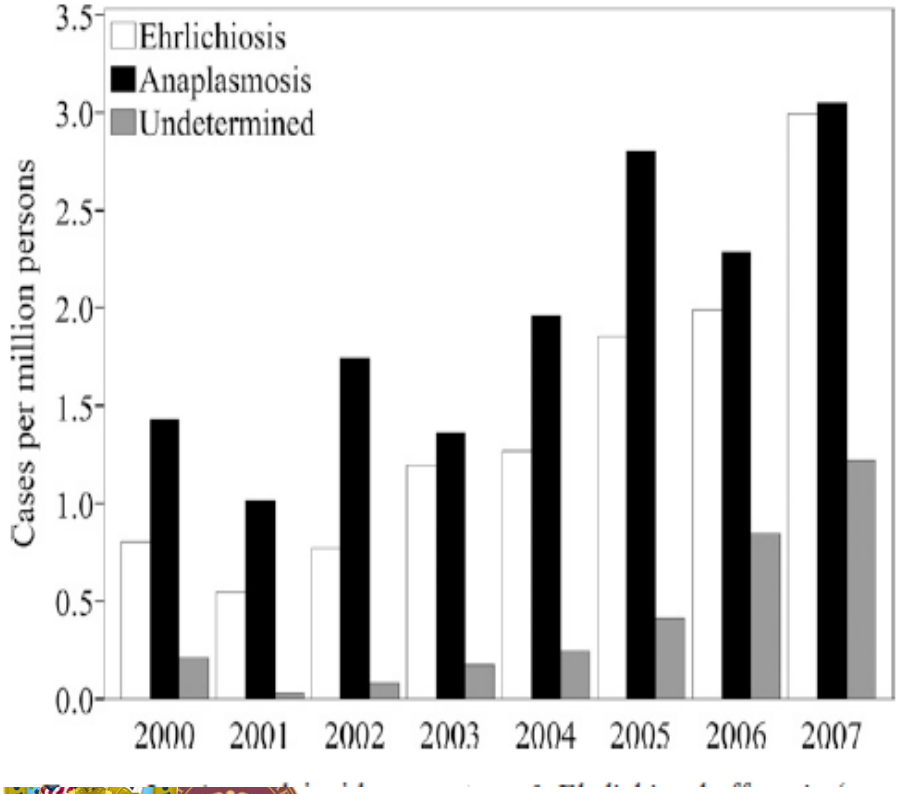
Clin Lab Med. 2010 March ; 30(1): 261–292. doi:10.1016/j.cll.2009.10.004.

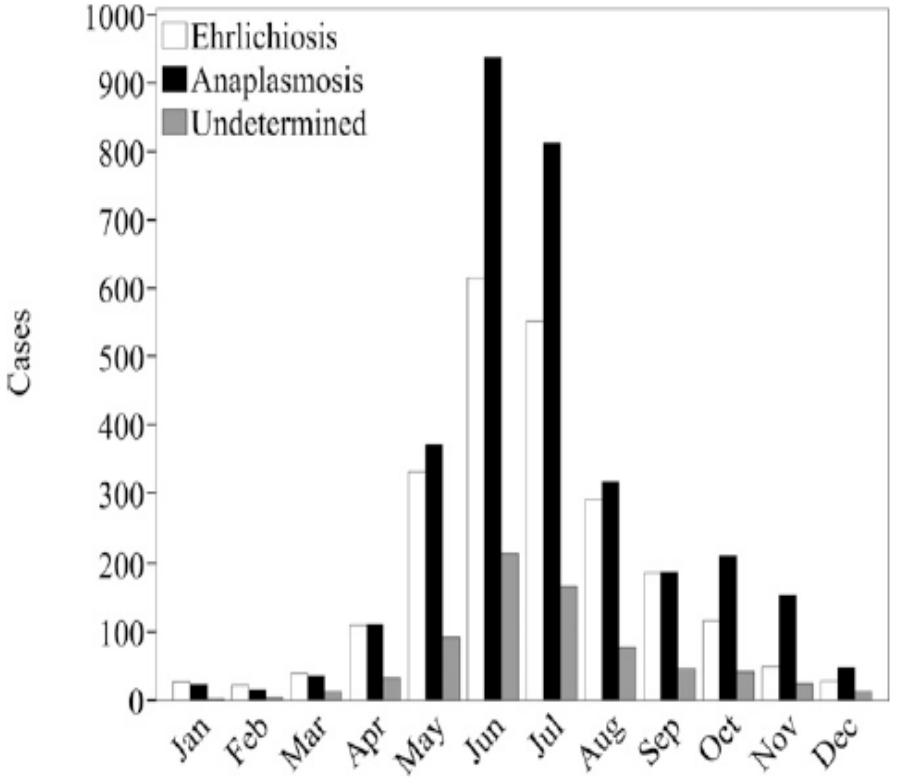
Am. J. Trop. Med. Hyg., 85(1), 2011, pp. 124–131
doi:10.4269/ajtmh.2011.10-0613

Increasing Incidence of *Ehrlichia chaffeensis* and *Anaplasma phagocytophilum* in the United States, 2000–2007

F. Scott Dahlgren, Eric J. Mandel, John W. Krebs, Robert F. Massung, and Jennifer H. McQuiston*

Division of Vectorborne Infectious Diseases, National Center for Enteric, Zoonotic, and Infectious Disease, Centers for Disease Control and Prevention, Atlanta, Georgia





Ehrlichiosis

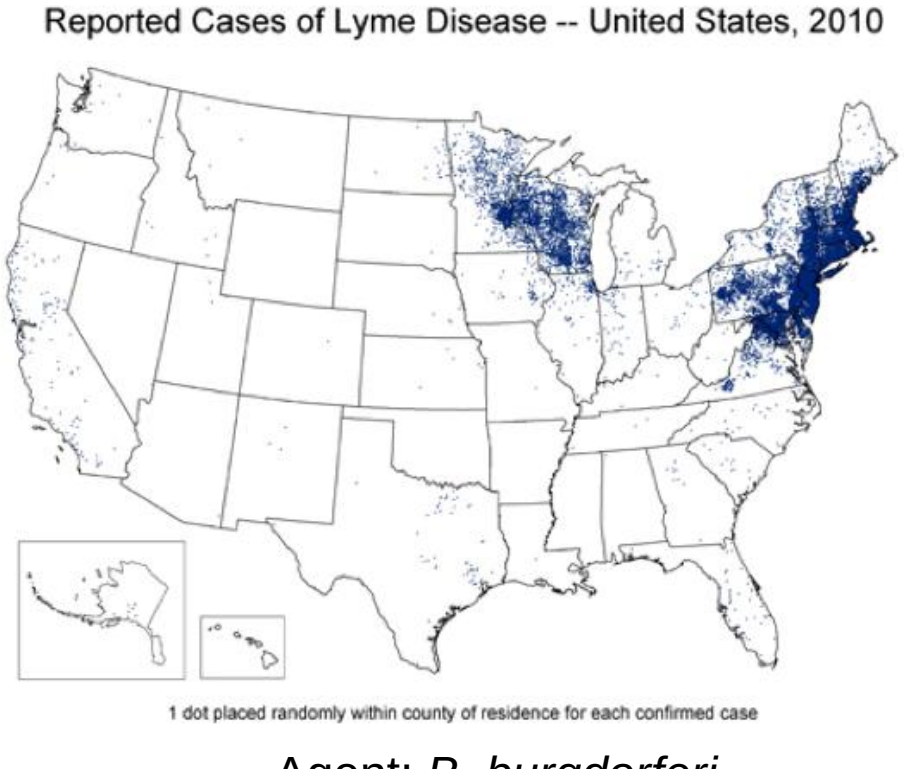
- Incubation 5-14 days
- Rash rare; NO vasculitis
- Ecology:
  - grassy areas, forest edge, un-mowed areas
  - May-Sept in USA
- Diagnosis: paired serology; peripheral blood smears (morulae=cytoplasmic inclusions); PCR
- Treatment: Doxycycline 100mg BID ~ 3d after afebrile (~5-7 days)
- Prevention: PPE

Ehrlichiosis and Anaplasmosis

Symptom, sign, or finding	Patients, % (no. evaluated) HME	HGA
Symptom or sign		
Fever	97 (633)	93 (521)
Myalgia	57 (250)	77 (516)
Headache	80 (240)	76 (385)
Malaise	82 (234)	94 (288)
Nausea	64 (143)	38 (258)
Vomiting	33 (192)	26 (90)
Diarrhea	23 (197)	16 (95)
Cough	26 (155)	19 (260)
Arthralgias	41 (211)	46 (504)
Rash	31 (286)	6 (357)
Stiff neck	3 (240)	21 (24)
Confusion	19 (279)	17 (211)
Laboratory finding		
Leukopenia	62 (276)	49 (336)
Thrombocytopenia	71 (247)	71 (336)
Elevated serum AST or ALT level	83 (276)	71 (177)

CID, 2007; 45 (Suppl

Lyme disease (*Borrelia* sp.)



Agent: *B. afzelii, B. garinii*
Vectors: *I. ricinus* – Europe
I. persulcatus – E. Europe, Russia

Agent: *B. burgdorferi*
Vectors: *I. scapularis* – East
I. pacificus - West

Lancet 2003; CDC.gov

Stages of Infection

Early Infection

- Rash (erythema migrans) in ~ 70-80%
  - At site of tick bite after 3-30 days
  - Gradually expands over several days
  - Central clearing (Bull's-eye-50% of time); warm but not painful
  - Occasional additional EM lesions days later
- +/- fatigue, chills, fever, headache, swollen lymph nodes

Late Infection

- Encephalomyelitis
- Carditis
- Arthritis in 60% untreated
  - Large and small joints, intermittent
  - Can develop chronic arthritis

Steere AC. *Borrelia burgdorferi (Lyme Disease, Lyme Borreliosis*) in *PPID*.2005.

Central clearing is not always present---look for unusual patterns or locations of cellulitis in summer months

Lyme Disease Manifestations

- Neuroborreliosis (5%)
  - Can occur at any time
  - Early: aseptic meningitis; cranial nerve palsies; peripheral neuritis/paresis
  - *Borrelia* DNA (PCR) in CSF
- Carditis
  - Conduction disturbances (AV block – complete block)
  - Check ECG if patient reports palpitations or syncope
- Arthritis
  - Intermittent attacks of inflammation
  - Synovial fluid positive for *Borrelia* DNA (PCR)
  - US>Europe

Steere AC. *Borrelia burgdorferi (Lyme Disease, Lyme Borreliosis*) in *PPID*.2005.

Table 3. Recommended therapy for patients with Lyme disease.

Indication	Treatment	Duration, days (range)
Tick bite in the United States	Doxycycline, 200 mg in a single dose[a,b]; (4 mg/kg in children ≥8 years of age) and/or observation	…
Erythema migrans	Oral regimen[c,d]	14 (14–21)[e]
Early neurologic disease		
Meningitis or radiculopathy	Parenteral regimen[c,f]	14 (10–28)
Cranial nerve palsy[a,g]	Oral regimen[c]	14 (14–21)
Cardiac disease	Oral regimen[a,c,h] or parenteral regimen[a,c,h]	14 (14–21)
Borrelial lymphocytoma	Oral regimen[c,d]	14 (14–21)
Late disease		
Arthritis without neurologic disease	Oral regimen[c]	28
Recurrent arthritis after oral regimen	Oral regimen[a,c] or parenteral regimen[a,c]	28 14 (14–28)
Antibiotic-refractory arthritis[i]	Symptomatic therapy[j]	…
Central or peripheral nervous system disease	Parenteral regimen[c]	14 (14–28)
Acrodermatitis chronica atrophicans	Oral regimen[c]	21 (14–28)
Post–Lyme disease syndrome	Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy[a]	…

IDSA Guidelines. Clin Infect Dis 2006;43:1089–134

Q fever (*Coxiella burnetii*)

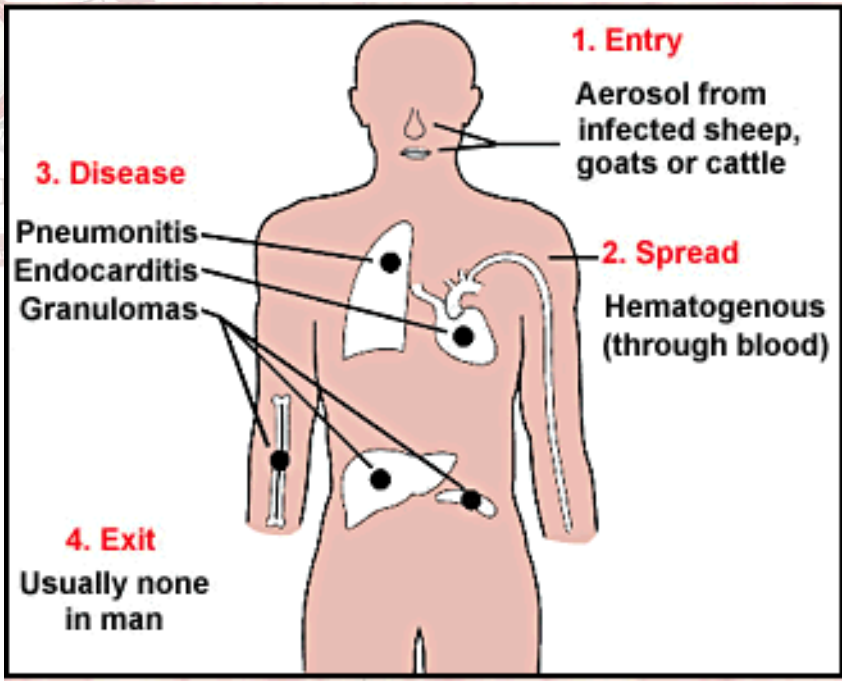
- Worldwide distribution
  - ↓ USA, ↑Netherlands, OIF
- Zoonosis: wildlife, ticks are main reservoir
- Transmitted from cattle, sheep, goats
  - Urine, feces, milk, birth products
  - Localizes to uterus/mammary glands
  - Via inhalation or ingestion
- Highly infectious
  - 1 organism can cause clinical infection

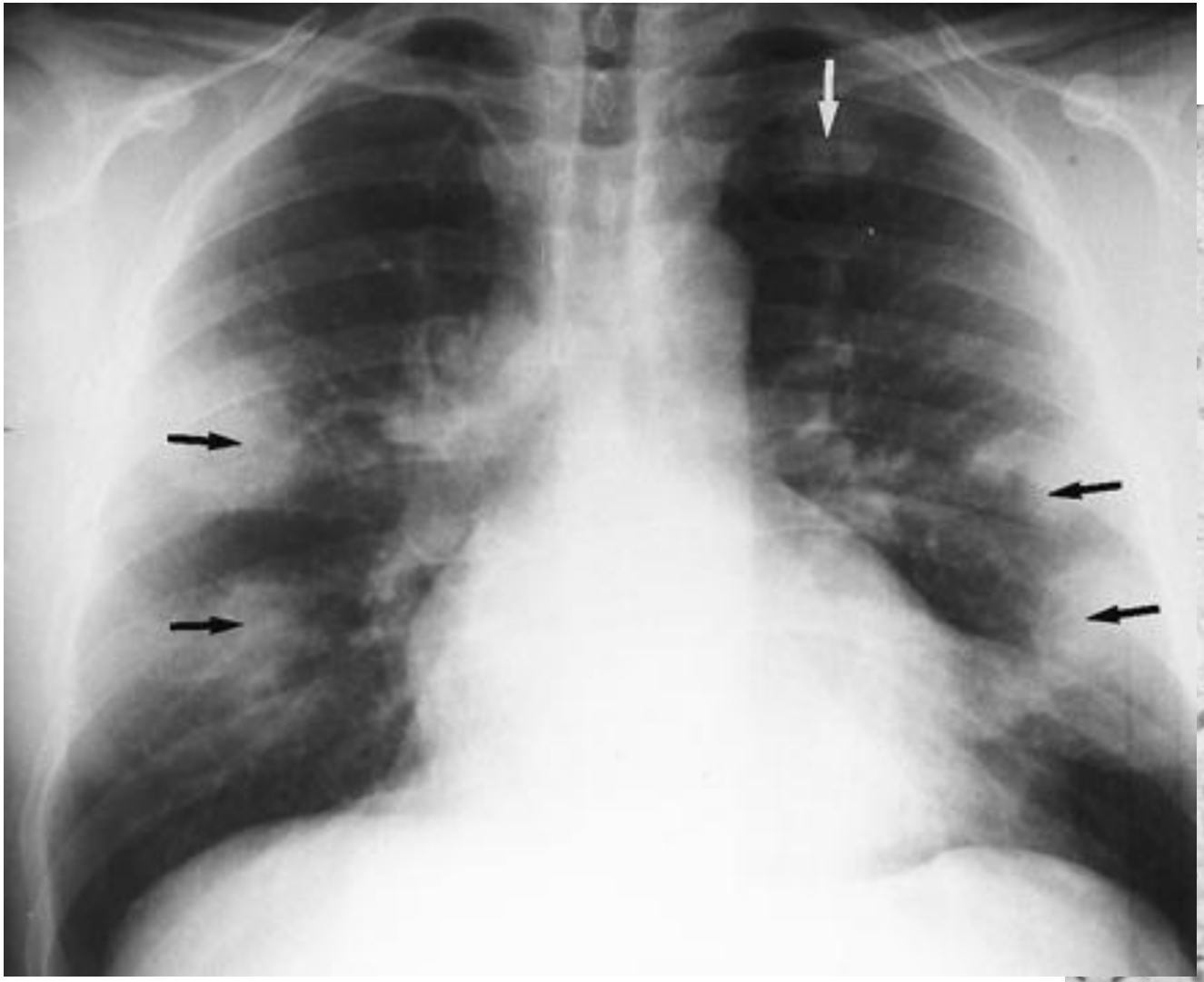
From Lancet 1984: 12 people were playing poker in the same room as a parturient cat. All 12 handled either the cat or litter and all 12 were diagnosed with acute Q fever (placentas carry 10^9 organisms).

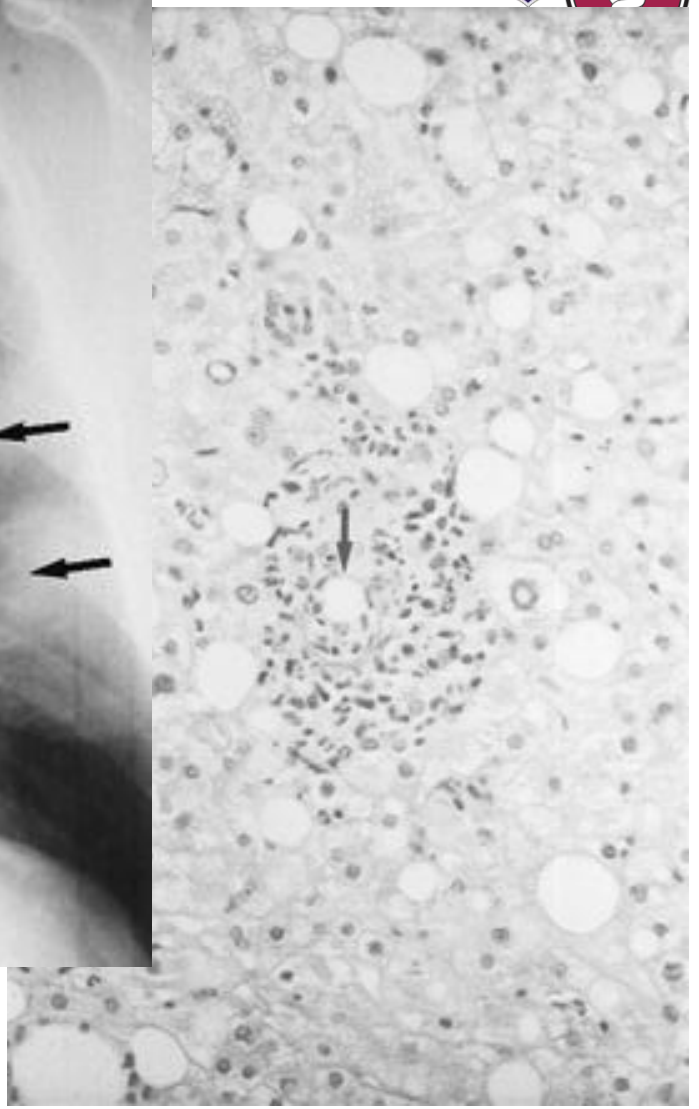
Q fever (*Coxiella burnetii*)

- 3 clinical presentations (major)
  - Febrile illness: self-limited; most common
  - Pneumonia (with fever): severe HA, retro-orbital pain
  - Hepatitis (with fever): “doughnut” granulomas”
  - * 60% asymptomatic

  Complications:
  - Endocarditis
    - Culture negative; chronic
  - Optic neuritis
  - Encephalitis







Q Fever (*Coxiella burnetii*)

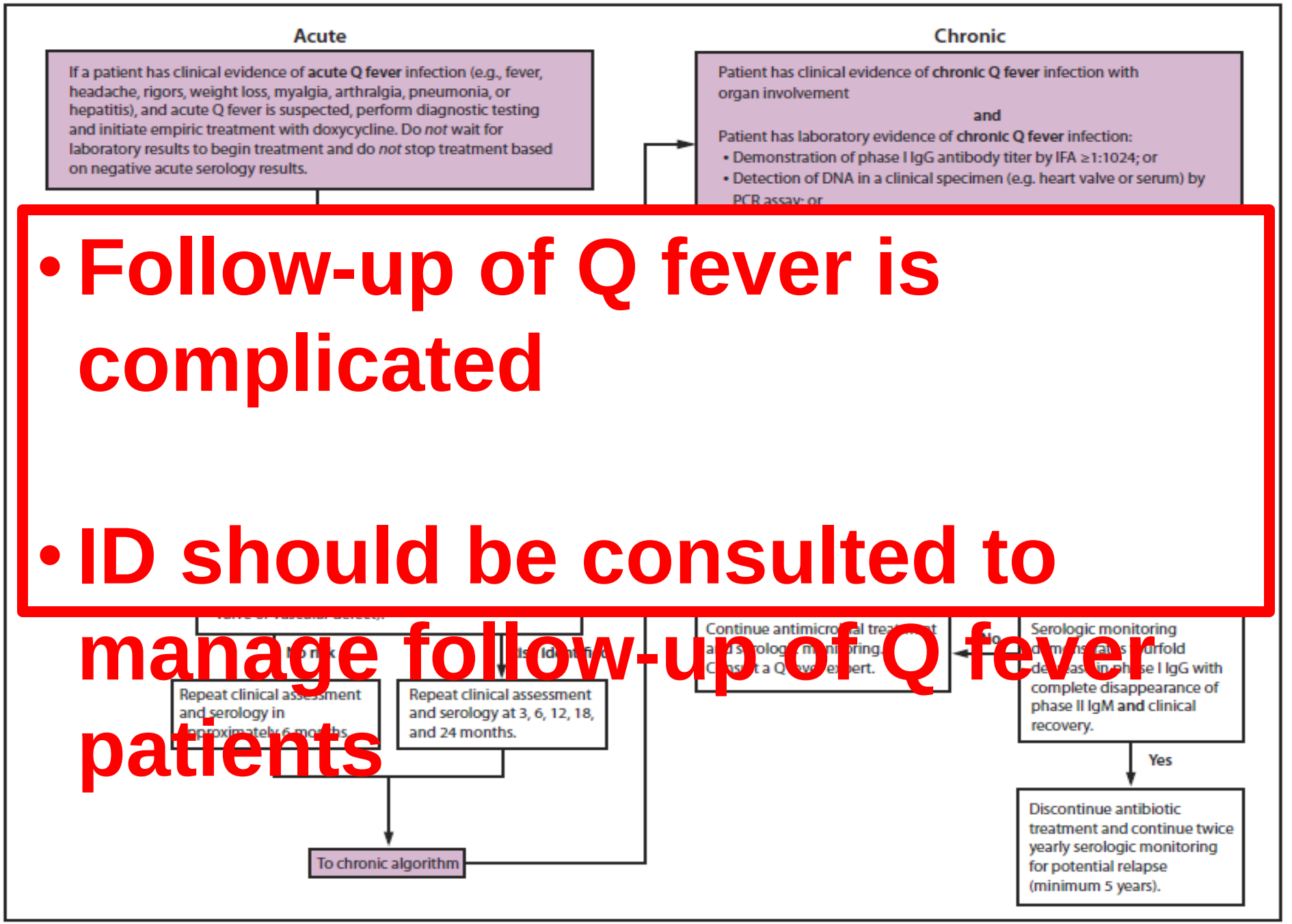
- Ecology: farmers, vets, abattoir/lab workers
- Diagnosis: paired serology
- Treatment:
  - Acute: Doxy x 14 days
  - Chronic/endocarditis: doxy + hydroxychloroquine x 18 mo.
- Prevention: educate (livestock, dairy)
  - Disposal of birth products (animals)
  - Quarantine/restriction of infected animals- Caution high risk patients (valve disease)

Diagnosis and Management of Q Fever — United States, 2013

Recommendations from CDC and the Q Fever Working Group

Anderson A. MMWR. 2013;62(3):1-28.

FIGURE. Q fever management algorithm*



- **Follow-up of Q fever is complicated**
- **ID should be consulted to manage follow-up of Q fever patients**

Matching

1. Rat-infested grain stores
2. Close living quarters, poverty
3. Sheep or cattle exposure
4. Transitional vegetation
5. Land navigation exercises

A. Spotted fever (*R. rickettsii*)
B. Q fever (*C. burnetii*)
C. Scrub typhus (*O. tsutsugamushi*)
D. Murine typhus (*R. typhi*)
E. Louse-borne Typhus (*R. prowazekii*)

Case #1

- 35yo USMC medic in Iraq x 7 months
- En route CONUS – fever 104°F
- Now daily fever/chills + retro-orbital HA, lower back and bilateral calf pain
- ROS: sore throat, watery diarrhea x 6 days
- Exposures: insect bites, slept in revamped Iraqi chicken factory, goats roaming, walked in brackish water, ate local Iraqi-prepared food

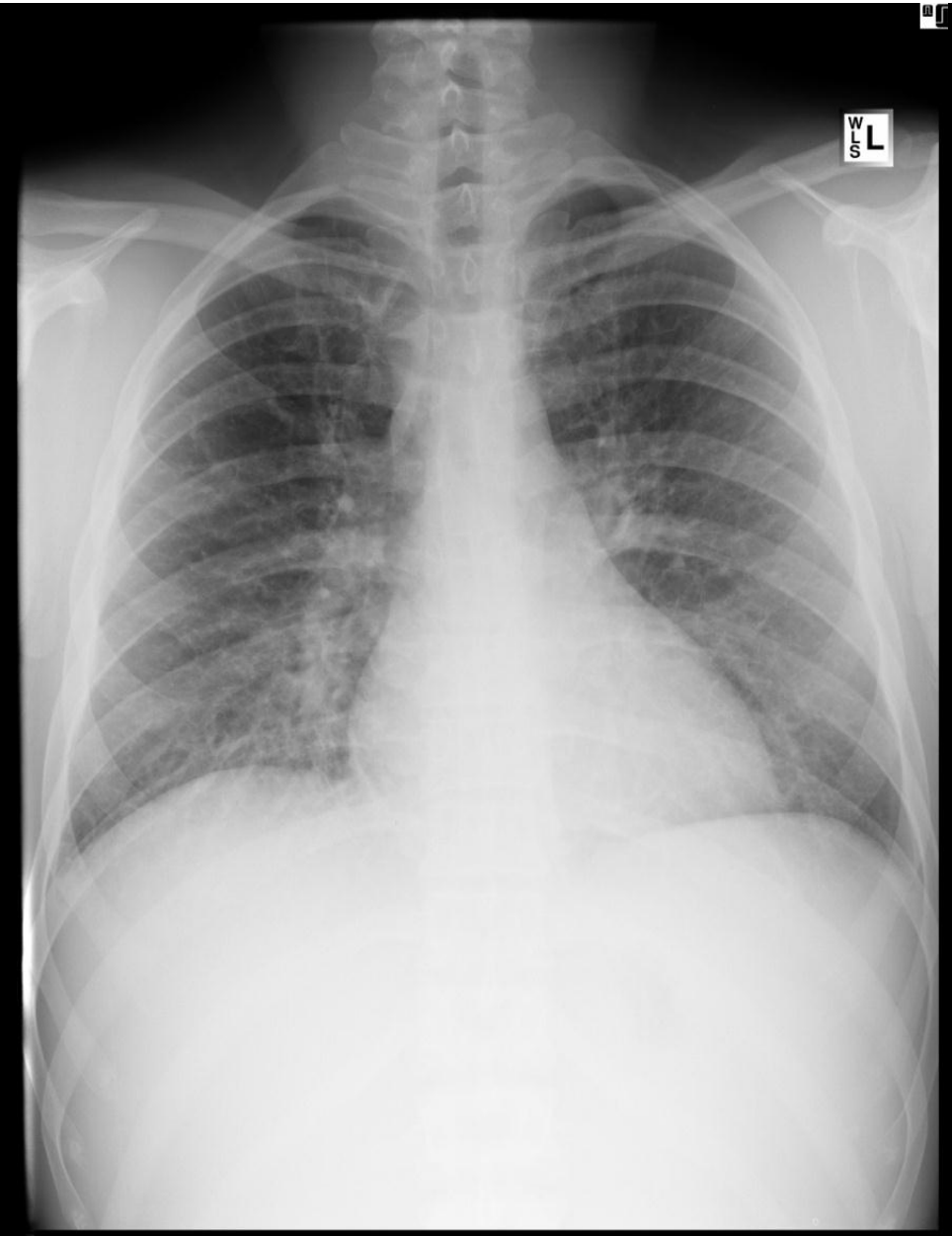
Case #1

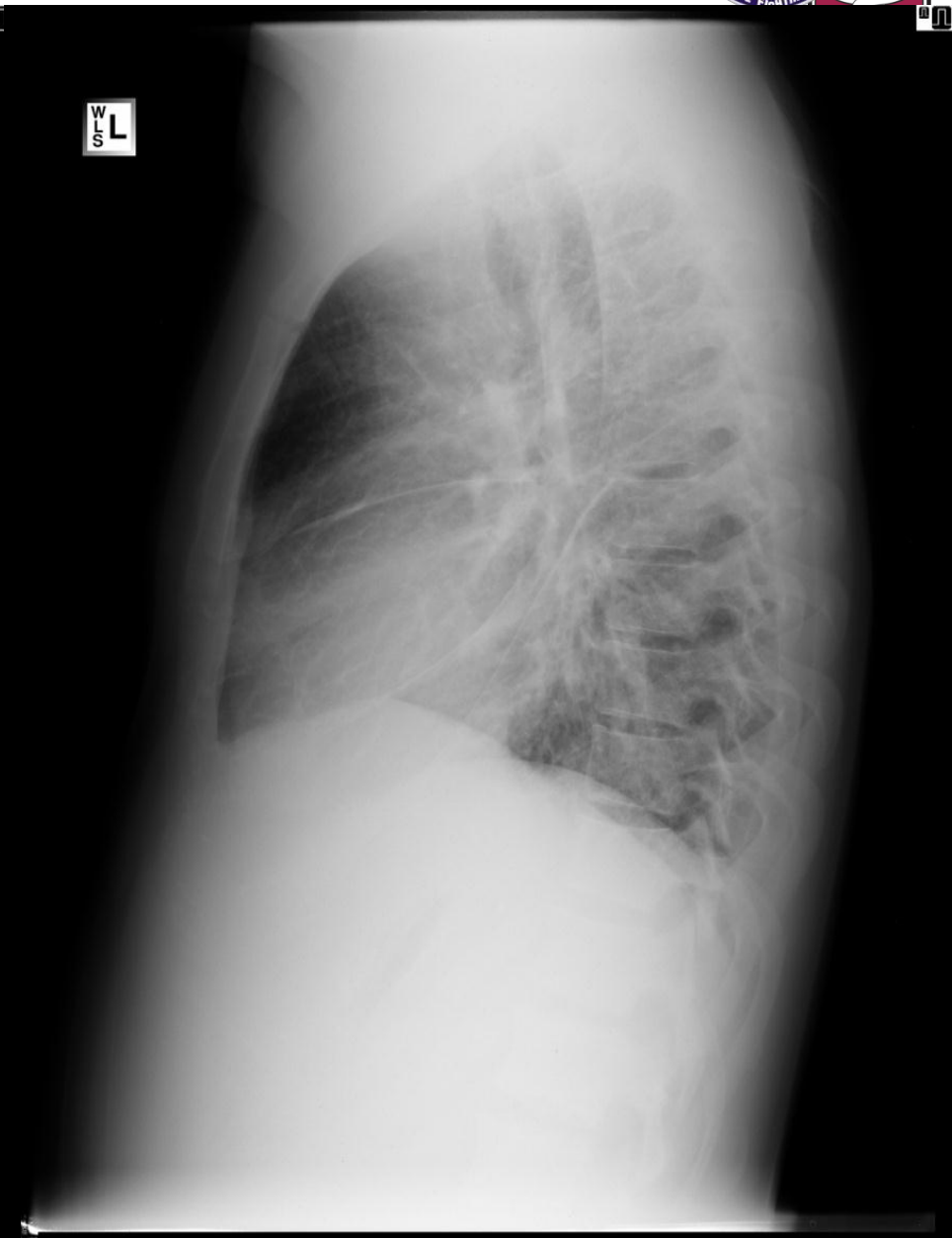
- PE:
  - T-103°F, HR-90, BP-110/60, O_2 Sat-99% (RA)
  - Unremarkable
- CXR, abdominal CT both normal

Case #1 part B

- 23yo USMC – becomes ill 3 days after #1
- Similar fever, chills, sore throat, diarrhea
- ROS: blisters on feet (waded through sewage); only ate MREs, did not sleep in chicken factory (500yds away)
- PE: T-106°F, HR-104, BP-120/70, O_2 Sat - 98%
  - Mild jaundice o/w normal

Case #1B





Lab data

- Patient 1
  - **Na-130** (137-145)
  - **K-3.0** (3.6-5.0)
  - **Alkphos**-310 (36-126)
  - **AST-125** (17-49)
  - **ALT-130** (7-56)
  - **Tbili 1.8** (0.2-1.3)
  - WBC 4.5 (4.0-11.0) 74N/E2
  - Plt-120 (150-450)
- Patient 2
  - **Na-130**
  - **K-2.9**
  - **Alkphos-137**
  - **AST-173**
  - **ALT-131**
  - **Tbili-2.8**
  - WBC-4.8
  - **Plt-45**

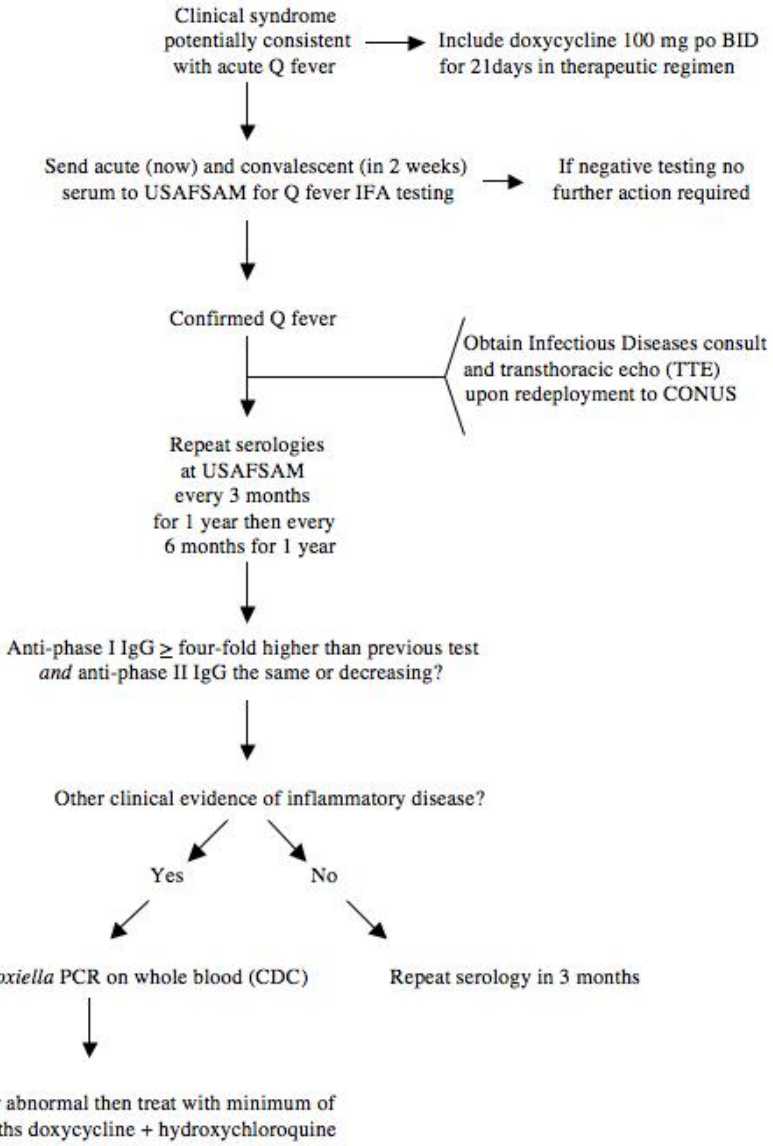
Case #1

- Differential?

- Malaria smears (-)
- Blood, stool, urine cultures (and CSF #1) (-)
- Acute HIV, RPR (-)
- Viral, Dengue, Hepatitis A/B/C (-)
- Leptospirosis Ab (-)

- **Q fever**

Current Recommendations of the Tri-Service Infectious Diseases Q Fever Working Group



Fevers, sweats, weight loss, chest pain, elevated erythrocyte sedimentation rate, C reactive protein, liver-associated enzymes, white blood cell count, rheumatoid factor

Case #2

- 44yo Indian subsistence farmer with fever x 7 days
- Fever unremitting, initially abrupt onset
- Previously well
- One day severe frontal HA, N/V, photophobia, DOE and now tender swelling in left groin

TAMIL NADU


ANDHRA PRADESH
KARNATAKA
KERALA
I N D I A
T A M I L N A D U
BANGALORE
CHENNAI
TIRUVALLUR
KANCHIPURAM
VELLORE
KRISHNAGIRI
DHARMAPURI
TIRUVANNAMALAI
VILUPPURAM
SALEM
NAMAKKAL
ERODE
PERAMBALUR
CUDDALORE
PONDICHERRY (PUDUCHCHERI)
NILGIRIS
COIMBATORE
TIRUCHCHIRAPPALLI
KARUR
THANJAVUR
THIRUVARUR
NAGAPPATTINAM
DINDIGUL
PUDUKKOTTAI
MADURAI
SIVAGANGA
TENI
VIRUDUNAGAR
RAMANATHAPURAM
TUTICORIN
TIRUNELVELI
KANNIYAKUMARI
THIRUVANANTHAPURAM
ERNAKULAM
KOTTAYAM
ALAPPUZHA
PATHANAMTHITTA
KOLLAM
PALAKKAD
THRISSUR
MALAPPURAM
KOZHIKODE
WAYANAD
KANNUR
KASARAGOD
MYSORE
MANDYA
CHAMRAJNAGAR
HASSAN
KOLAR
TUMKUR
BAY OF BENGAL
INDIAN OCEAN
Gulf of Mannar
Palk Strait
Palk Bay
SRI LANKA
Jaffna
Point Pedro
Elephant Pass
Kankesanturai
LEGEND
State Boundary
District Boundary
National Highway with no.
Major Roads
Railway Line
State Capital
Union Territory Capital
District Headquarters
Other Towns
Tourist Places
Airport
Seaport
Cartographed By Vishnu Maps Publications. Chennai - 600 033
Ph : 044-24712939
Not to Scale

ROS

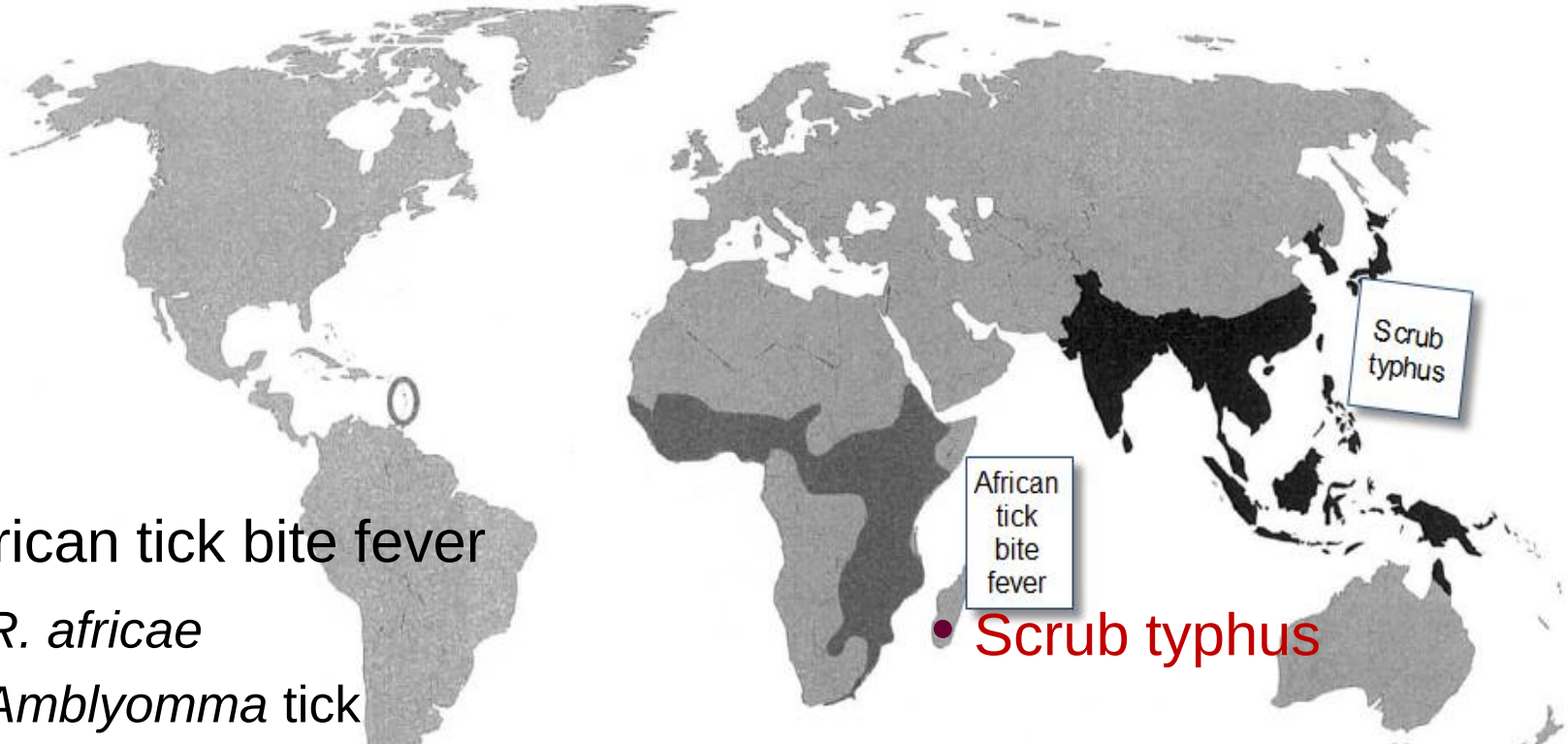
- No travel
- Chickens on farm
- Married, 2 children – all healthy
- Vegetarian; makes yogurt
- Water – well or river (wife gathers)
- No TOB, ETOH, drugs, meds, allergies
- Childhood vaccines (WHO) completed

Courtesy: N. Aronson, MD

More clinical information

- Following incubation (6-21 d), sx appear
- After initial sx (F, HA, chills, fever, ↓ hearing, conjunctivitis/suffusion, LAD), ulcer seen then centrifugal rash within 1 wk
- 2nd wk (if untreated):
  - Splenomegaly
  - Pneumonia
  - Myocarditis
  - Delirium
  - Death
- Diagnosis?

Scrub Typhus



- African tick bite fever
  - *R. africae*
  - *Amblyomma* tick
  - ↑ tourists (~5%)
  - HA, myalgias, eschar/s
  - Vesicular rash, mouth blisters 30%
  - Reactive arthritis (5%)
  - Self-limited

- Scrub typhus
  - *Orientia tsutsugamushi*
  - Mites
  - Loggers, rice farmers, military
  - F, LAD (70%), eschar (50%)
  - **PNA**, CNS, DIC, renal failure
  - Indep. predictor mort: met. acidosis (↑ ast, wbc, ↓ plt)

Case #3

40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

A. Doxycycline

B. Atovaquone

C. Azithromycin

D. Gentamicin

40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

A. Doxycycline

B. Atovaquone

C. **Azithromycin**

D. Gentamicin

Case #4

A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

A. Ehrlichiosis
B. Spotted fever group rickettsiosis
C. Bartonellosis
D. Typhus group rickettsiosis

A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

A. Ehrlichiosis

B. Spotted fever group rickettsiosis

C. Bartonellosis

D. Typhus group rickettsiosis

#5

Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

A. Tetracycline
B. Minocycline
C. Septra
D. Doxycycline

Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

A. Tetracycline
B. Minocycline
C. Septra
D. Doxycycline

#6

During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

A. *Orientia tsutsugamushi*
B. *Rickettsia rickettsii*
C. *Rickettsia prowazekii*
D. *Rickettsia typhi*

#6

During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

A. *Orientia tsutsugamushi*

B. *Rickettsia rickettsia*

C. ***Rickettsia prowakezii**

D. *Rickettsia typhi*

Location, location, location…

Rickettsial disease	Geographic locations where most prevalent
RMSF	•Primarily in the continental United States and rarely elsewhere
Rickettsialpox	•Large cities in Russia, South Africa, and Korea
Boutonneuse fever	•Mediterranean countries, such as Spain, Italy, and Israel
Louse-borne typhus (Epidemic) Brill-Zinsser disease	•Europe, Asia and Africa •In the last 2 decades African countries, especially Ethiopia and Nigeria, have reported most cases
Murine	•Large cities around the world with high rate infestations
Tsutsugamushi disease	•Japan, Solomon Islands and Pakistan
Q fever	•Australia, Canada and other parts of the world where humans come into contact with infected animals

Transmission

Disease	Causative rickettsia	Transmitting vector/carrier
Rocky Mountain Spotted Fever (RMSF)	*R rickettsii*	Vector: wood tick, dog tick, and Lone Star tick Humans become incidental host after being bitten by infected adult tick
Rickettsialpox	*R akari*	Vector: house mouse is the natural host of the mouse mite transmitting rickettsialpox Distribution: Russia, South Africa, Korea
Boutonneuse fever	*R conorii*	Vector: various ticks including dog ticks
Louse-borne typhus	*R prowazekii*	Vector: Human lice
Brill-Zinsser disease	*R prowazekii*	Vector: lice Reactivation of the organism from a latent state up to decades after primary infection
Murine	*R typhi* and *R felis*	Transmitted between rats by a rat flea Humans accidentally infected by the faeces of infected fleas
Tsutsugamushi disease	*O tsutsugamushi*	Vector: larval trombiculid mites in soil and scrub
Q fever	*C burnetii*	Vector: Airborne droplets from infected cattle , sheep goats, rodents and cats Slaughterhouse and animal research workers at risk Ticks transmit disease to rodents and domestic animals but are seldom the cause of human infection Organism remains latent in infected host until stressor such as birth activates it. Then multiplies and contaminates animals' surrounding, persisting as

Table II. Differential diagnosis of an eschar

Infectious

- Bacterial: ecthyma caused by Staphyloccocus or Streptococcus, ecthyma gangrenosum, necrotizing fasciitis, anthrax, glanders, plague, phagedenic ulcer, rat bite fever, tularemia
- Viral: orf/milker's nodule, herpes simplex virus
- Rickettsial: scrub typhus, the spotted fever group including rickettsialpox, South African tick bite fever, Siberian tick typhus, Queensland tick typhus, and boutonneuse fever
- Fungal: aspergillosis, fusariosis, mucormycosis

Inflammatory

- Brown recluse spider bite
- Thrombotic disease: antiphospholipid syndrome ulcers, coumadin and heparin necrosis, calciphylaxis

Summary

- Rickettsial diseases have nonspecific symptoms
  - Fever, headache, abnormal LFTs, thrombocytopenia
- Thorough skin exam: look for eschars
- Rashes are not always present
- Get a good travel history
- Know what is endemic where you are
- Mortality is high for some conditions
- Treat with doxycycline when in doubt

NO ONE DIES WITHOUT DOXYCYCLINE ON BOARD!!

WRAIR

Walter Reed Army Institute of Research

Soldier Health • World Health

QUESTIONS?